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HEXAMETHYLENAMIN IN THE TREATMENT OF SYSTEMIC INFECTIONS WITH A SPECIAL EMPHASIS UPON ITS USE AS A PROPHYLACTIC.

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The suggestion that hexamethylenamin be used in the treatment of systemic infections is based entirely on the results of experimental and clinical observations; and the object of this publication is to call attention to the fact that this drug is of value, not only as a therapeutic, but especially as a prophylactic measure, in a great variety of maladies. Among the conditions which may be favorably influenced by the administration of hexamethylenamin, the following are the most important:

(1) Infections of the genito-urinary tract and typhoid bacilluria.

(2) Infections of the bile ducts and gall bladder.

(3) Infections of the cerebro-spinal system, poliomyelitis, epidemic meningitis, meningeal infections following injuries or infectious processes elsewhere in the body.

(4) Infections of the respiratory tract, including infections of the para-nasal sinuses and ears, acute rhinitis, acute tonsillitis, and some forms of bronchitis. (In lobar pneumonia and pulmonary tuberculosis it is doubtful whether this drug is of any value.)

Hexamethylenamin, itself, is well known to practitioners in all parts of the world as the best of the genito-urinary antiseptics. It is sold under various proprietary names; such as, urotropin, helmitol, cystogen, formin, uratone, etc.[1] Hexamethylenamin is prepared by the action of formaldehyde on ammonia, and owes its value as a therapeutic agent to the fact that it undergoes decomposition in the body liberating free formaldehyde. This fact was first noted in 1895 by Nicolaier.[2] After the administration of hexamethylenamin (urotropin) in doses of three to six grams (45 to 60 grains) a day, Nicolaier found that this drug, or its decomposition product formaldehyde, invariably appears in the urine in amounts which suffice to markedly inhibit the growth of organisms—even when a voided specimen of urine is directly inoculated (with streptococcus) and kept under the most favorable cultural conditions. In 1898, Richardson[3] called attention to the fact that post-typhoid bacilluria may be prevented by the daily administration of small amounts of hexamethylenamin throughout the course of typhoid fever.

[1] Although certain of these preparations are less irritant, there are none which liberate more formaldehyde than does the chemically pure hexamethylenamin.

[2] Nicolaier: Deutsche med. Wchnschr., 1895, XXI, 541-543; Deutsches Arch. f. klin. Med., 1904, LXXXI, 181-223.

[3] Richardson: J. Exp. M., 1899, IV, 19.

Further investigations, however, concerning the pharmacology of hexamethylenamin, were not made until 1908; in this year some experimental studies,[4] carried out in the pharmacological laboratory of the Johns Hopkins University, disclosed the fact that this drug is not excreted by the kidneys alone, but that within a short time after its administration by mouth it may be demonstrated in practically *all* of the body fluids.

The presence of hexamethylenamin, or formaldehyde, in a given secretion may be quickly determined by a simple chemical test.[5] By employing this test it was found that hexamethylenamin is invariably excreted into the bile, pancreatic juice, cerebro-spinal fluid, saliva and milk. It may also be demonstrated in synovial, pleural and peritoneal effusions, and in the circulating blood. It finds its way into the bile both through the liver and through the wall of the gall-bladder, as may be shown by administrating the drug to an animal after a preliminary ligation of the cystic duct, and testing separately the bile escaping through the common duct and that contained in the gall-bladder. Aside from the single, isolated observation of Bucura,[6] in 1907, that hexamethylenamin is excreted in the milk, it had not been recognized that this drug appeared in any of the body fluids other than the urine and circulating blood.

Following our experimental studies in 1908, some investigations made on clinical cases, in which it was possible, due to the presence of a post-operative biliary fistula, to make cultures and obtain specimens of bile directly from the interior of the gall-bladder, disclosed the following facts:

(1) Hexamethylenamin, given either by mouth or by rectum, makes its appearance in the bile and in the urine almost simultaneously.

[4] Crowe: Johns Hopkins Hosp. Bull., 1908, XIX, 109. Arch. Internat. de Pharmacodyn. et de Thérap., 1908, XVIII, 315.

[5] Hexamethylenamin undergoes decomposition so readily that it may be said to respond to all the formaldehyde tests with which we are acquainted. By the well-known reaction with bromine water (tetrabromhexamethylenamin appears as a precipitate), it is easy to demonstrate the presence of hexamethylenamin in a given excretion, but this test throws no light whatever on the presence of formaldehyde. The modified Hehner's test has proven to be the most satisfactory, although it is purely a formaldehyde test. Formaldehyde is liberated by the catalytic action of sulphuric acid on hexamethylenamin, and in the presence of a small amount of casein a deep amethyst color is developed. In clear solutions, such as the urine, pancreatic juice and cerebro-spinal fluid, or by using the distillates of bile or purulent effusions, the approximate concentration of the drug may be determined by comparing the color with that given by a formaldehyde solution of known strength. The method of applying the test is as follows: To the colorless fluid to be tested a drop or so of milk or a very small amount of casein is added, and this mixture stratified with an equal volume of the reagent, which is composed of 100 cc. of 99 per cent sulphuric acid and one drop of a 3 per cent ferric chloride solution. A deep amethyst color develops at the juncture of the layers and may be diffused by shaking. If formaldehyde (hexamethylenamin) is present in too great a concentration, however, the color reaction may not occur without dilution of the fluid.

[6] Bucura: Ztschr. f. exp. Path. u. Ther., 1907, IV, 398.

(2) Provided large doses of hexamethylenamin are given, at least 75 grains a day, this drug appears in the gall-bladder in a concentration which suffices to render the bile an unsuitable media for the growth of bacteria.

In some of the cases, in which the infecting organism was *B. typhosus*, it was possible, by the simple administration of hexamethylenamin, to render the interior of the gall-bladder sterile—at least so long as active therapy was continued. These results led us to conclude that hexamethylenamin would be of great value in the prevention and treatment of acute infections of the bile passages, and that it should always be given as a protective measure before operations on the gall-bladder or bile ducts.

Since it has been repeatedly shown that the spread of typhoid fever is largely due to infected excretions, and that the relapses occurring during the course of this disease are due to some locally persisting infection, not infrequently situated in the gall-bladder, we strongly recommend that large doses of hexamethylenamin be given throughout the course of typhoid fever as a prophylactic measure. As will be shown in discussing the toxicity of hexamethylenamin, this drug has, in the majority of cases, no untoward effects if given in small doses, at frequent intervals, and sufficiently diluted with liquids.

Our investigations during the past four years have been chiefly directed toward the experimental and clinical study of the value of hexamethylenamin in threatened or actual cerebro-spinal infections. There are a great variety of conditions, such as compound fracture of the skull (especially if the fissure passes through the middle ear or cribriform plate), infections of the scalp, acute infections of the ear or accessory nasal sinuses, or certain operative procedures which may be followed by an infection of the cranial cavity, in which it is especially desirable to have some measure for combating a secondary infection of the meninges. Also the number of reported cases of intra-cranial complications—meningitis, abscess and sinus thrombosis—which have followed a primary inflammatory process in the nasal cavities or para-nasal sinuses, now form an extensive series. Moreover, it has been shown by Flexner, and others, that both the meningococcus and the virus of poliomyelitis appear to have a predilection for invasion of the mucous membrane of the naso-pharynx, and from there to pass, presumably by the lymphatics, to the central nervous system. Post mortem studies in poliomyelitis, however, have shown that in both the experimental and the epidemic cases there is always an inflammatory reaction of the meninges preceding the invasion of the nervous system; thus holding out some hope that when the early symptoms of this disease are recognized, its further progress may be arrested by the administration of a drug which will be excreted into the cerebro-spinal fluid, and so render this fluid an unsuitable media for the continued growth of the virus.

That hexamethylenamin might actually be of value in the prevention and treatment of meningeal infections was first suggested to me by Dr. Harvey Cushing. This supposition was

confirmed by some experimental observations,[7] made in 1909, from which the following conclusions may be drawn:

(1) Hexamethylenamin, given either by mouth or by rectum, invariably appears in the cerebro-spinal fluid, both in man and in animals.[8] By comparative chemical tests it was determined that the concentration of hexamethylenamin in the cerebro-spinal fluid reaches its height from thirty minutes to an hour after its administration. This point is of the greatest practical importance in determining the frequency with which this drug should be given in cases with a meningeal infection, and will be fully discussed in a later section.

(2) After doses of hexamethylenamin, within therapeutic limits, a sufficient amount of the drug appears in the cerebro-spinal fluid to have a marked inhibiting effect on the growth of organisms (streptococcus) inoculated into this fluid after its removal from the body.

(3) Following a subdural inoculation of dogs and rabbits with a virulent culture of streptococcus, sixty to eighty grains of hexamethylenamin a day, given under conditions which insure absorption, will markedly defer, and in some cases prevent the onset of a fatal meningitis. This conclusion is based on the results of forty experimental observations. In each experiment four animals were used. The dura in each animal was exposed, under aseptic precautions, by a trephine opening in the broad posterior arch of the atlas, and 0.1 cc. of a boullion culture of streptococcus was injected into the cerebro-spinal space. One animal in each experiment was used as a control; the other three receiving hexamethylenamin under varying conditions and in varying amounts. In no case did the control animal survive longer than thirty-six hours, and on examination a diffuse, purulent meningitis was found; in many of the others the progress of the infection was held in abeyance during the continuance of active therapy, but as soon as the drug was withdrawn the organisms immediately began to multiply, with a return of clinical symptoms.[9] A few of our animals, however, made a complete recovery after a prolonged and careful treatment; and at autopsy, several weeks later, no trace of an infection could be seen, other than a slight thickening of the meninges near the point of inoculation. It is worthy of note that the only animals which recovered after a direct subdural inoculation were those to whom large doses of hexamethylenamin were given, as a *prophylactic* measure, for several days preceding the inoculation.

[7] Crowe: Johns Hopkins Hosp. Bull., 1909, XX, 102.

[8] From a pharmacological standpoint it is interesting to note that hexamethylenamin is the only substance known which is excreted into the cerebro-spinal fluid in amounts sufficient to be of the slightest therapeutic value. Of the inorganic substances, the bromides, mercury and lead do not appear in the cerebro-spinal fluid; potassium iodide, lithium and thallium have been found in very minute traces. Of the organic substances, traces of acetone have been found in the cerebro-spinal fluid of severe cases of diabetes with acetonuria; also chloroform may appear in minute quantities after a prolonged anæsthetization. Salicylic acid compounds are not excreted in the cerebro-spinal fluid. Bile pigments and dyes, with the exception of pyrrol-blue, and many of the toxins and immune bodies present in the blood serum may not be demonstrated in the cerebro-spinal fluid. Urotropin, however, invariably appears, and after therapeutic doses, in man, has been found in a concentration of 5 cg. to the liter. (Hald: Arch. f. exper. Path. u. Pharm., 1911, LXIV, 329.) This also furnishes a good example of the specific properties of endothelium.

[9] This is much the same experience that has long been had with hexamethylenamin in the treatment of genito-urinary infections, and we have had a similar outcome in two clinical cases of meningitis in which it was necessary, on account of the bladder irritation and hematuria, to withdraw the drug.

CLINICAL EXPERIENCES.

Since 1908, it has been a routine measure in the Johns Hopkins Hospital to administer hexamethylenamin to all cases in which a meningeal infection is a possible or threatened complication. Quite an extensive series of such cases have been studied during the past three years, and the results seem to definitely establish the therapeutic and prophylactic importance of this drug. This series includes cases of:

(1) Compound fracture of the skull.
(2) Tumors of the hypophysis with neighborhood symptoms necessitating operative procedures through the nose.
(3) Post-operative cerebro-spinal fistulæ.
(4) Infections of the ear and para-nasal sinuses.
(5) Acute poliomyelitis.

FRACTURES OF THE SKULL.

The serious nature of compound fractures of the skull lies not only in the possibility of an intracranial bleeding, but in the extreme likelihood of infectious meningitis or cerebral abscess following the inoculation of septic material. As a rule, fractures of the base are attended with a higher mortality than are those of the vault, since an insignificant fissure which passes across the ethmoid plate may open a pathway of infection from the nasal cavity. Not infrequently a rapidly fatal pneumococcal meningitis may start up on the third or fourth day after what appears to be a simple, uncomplicated basal fracture with but few, if any, subjective symptoms.

With the hope of preventing complications of this character, we have, during the past three years, given hexamethylenamin as a routine measure to all patients admitted to this hospital with an injury of the head. There have been thirty-five consecutive cases of undoubted basal fracture, with bleeding, or escape of cerebro-spinal fluid from the nostrils or ears, without a single instance of a secondary meningeal infection.[10] There were, however, nine deaths ascribed to meningeal infection or brain abscess among the thirty-five earlier cases of basal fracture to whom hexamethylenamin was not given.

During the past five years there have been twenty cases of compound fracture of the vault, similar, in that there was a laceration of the meninges and underlying cortex in each in-

[10] Many of these patients are unconscious when brought to the hospital, others have nausea and vomiting to such a marked degree that it is inadvisable to give liquids by mouth; in these cases the hexamethylenamin is administered per rectum, from thirty to sixty grains being dissolved in 300 cc. of salt solution, or plain tap water, and allowed to slowly flow into the bowel.

stance. In eight of the earlier cases hexamethylenamin was not given and the mortality from infection was fifty per cent.[11] To each of the remaining twelve cases, hexamethylenamin was given immediately after the injury, and at frequent intervals until all danger of infection was past; ten of these patients recovered, while two succumbed with a pneumococcal meningitis.

In one of these fatal cases there was an extensive depressed fracture of the skull and foreign matter had penetrated far into the cortex. At operation the wound was cleansed as well as possible and adequate drainage established. For ten days the symptoms of an intracranial infection were held in abeyance by the administration of from 120 to 140 grains of hexamethylenamin a day. At the end of this time, however, it was necessary to temporarily withdraw the drug on account of painful micturition and hematuria.[12] The general condition of the patient rapidly became worse and death occurred thirty-six hours later; the autopsy disclosed a diffuse, suppurative meningitis. We have several times had a similar experience with hexamethylenamin in experimentally produced cerebral infections in animals; and it is well known that in chronic infections of the urinary bladder the symptoms may temporarily subside, but tend to reappear soon after the inhibiting influence of the drug has been removed.

Although it is difficult to ascribe the recovery in an individual case to any particular form of therapy, still in view of our experimental observations, it seems justifiable to give the following histories, as examples of the prophylactic and therapeutic value of hexamethylenamin in meningeal infections.

Compound Fracture of the Skull; Cerebro-spinal Rhinorrhœa for 25 days; Recovery. Average amount of Hexamethylenamin 70 grains a day (for 28 days); no toxic effects.

Surgical No. 23467. F. L., a laborer, 30 years of age, was brought to the Johns Hopkins Hospital, on January 15, 1909, in an unconscious condition. About two hours before admission he had fallen from a travelling crane into a pile of scrap-iron twenty feet below. There was a large, jagged wound running from the right temporal region into the external canthus and across the right upper lid to the root of the nose. Through the center of this dirty wound, which had been bleeding profusely, there was a constant oozing of cerebro-spinal fluid and fragments of cortex. At operation the wounds were cleansed as well as possible, the bleeding controlled and protective drains inserted.

For the first three days approximately 100 grains of hexamethylenamin, well diluted, was given every twenty-four hours. On the day following the accident the temperature was 102° F. and the leucocytes numbered 20,800; two days later the leucocytes were 8,600 and thereafter remained within normal limits. The temperature slowly fell to normal and at no time was there any evidence of a meningeal infection. The lacerated wounds on the face healed rapidly, but there was a constant escape of cerebro-spinal fluid from both nostrils for twenty-five days. For twenty-eight days the average daily amount of hexamethylenamin was 70 grains a day; at no time, however, was there the slightest evidence of digestive disturbances or renal irritation.

Bursting Fracture of the Skull with Local Depression over Left Frontal Lobe; Simple Fracture of One of the Small Bones of the Hand; General Streptococcus Septicæmia; Cerebral Abscess; Meningitis; Recovery.

Surgical No. 26092. William P., age 7½. Admitted to the Johns Hopkins Hospital on June 13, 1910, with the following history: Three days previously was struck, from behind, by an automobile and thrown violently to the pavement. For an hour the patient was unconscious, and vomited once about four hours after the accident, but as there was no scalp wound other than a superficial abrasion over the left eye, and no bleeding from the nose or ears, the injury was not regarded as serious. The following day, however, the temperature suddenly rose to 103.4° F. On admission to the hospital, 48 hours after the injury, there was definite rigidity of the muscles of the neck, a positive Kernig's sign, a leucocytosis of 26,000, a low grade of choked disc and a temperature of 105° F. The cerebro-spinal fluid was cloudy and contained many pus cells; cultures showed the infecting organism to be a streptococcus.

On inquiring into the past history it was found that the child had had frequent attacks of tonsillitis and for several days preceding the accident had been feverish and complaining of a sore throat. On examination the whole throat was found to be inflamed, and there were small patches of exudate on the tonsils; a smear showed that the predominating organism here also was a streptococcus.

A decompressive opening was made under the temporal muscle on the left side but without disclosing any abnormality other than a tense œdematous brain. An incision into the bruised area over the left eye, however, unexpectedly disclosed a fracture from which pus exuded, and on further investigation a definite cavity was found in the left frontal lobe, from which there was an escape of infected, fragmented, cortical substance. Two days later the operative wound became infected and opened; a streptococcus abscess also developed around a fractured metacarpal in the right hand. Both infections were evidently hematogenous in origin, since there was no abrasion of the skin overlying the injury in the hand, and a streptococcus was recovered in cultures from the circulating blood.

Subsequent Therapy.—With the exception of the decompressive operation, and a lumbar puncture on three occasions for diagnostic purposes, an almost continuous administration of hexamethylenamin constituted the only treatment given in this case. From June 13 to July 4 (22 days) this child—7½ years of age—was given 939 grains of hexamethylenamin, a daily average of 42½ grains. During the first forty-eight hours after admission 291 grains were given, but insufficiently diluted with water, and on the following day the urine contained red blood cells and albumen. The additional administration of 100 grains on June 17 was followed by a marked hematuria, nausea and vomiting. The urine rapidly became normal, however, and the gastric symptoms entirely disappeared on withholding the drug for twenty-four hours and forcing liquids. Unfortunately, observations were not made to determine the concentration of the drug in the cerebro-spinal fluid or the circulating blood, or to follow by daily cultures its effect upon the organisms in either of these situations.

The following table illustrates the method which we employ in giving large doses of hexamethylenamin. Aside from personal idiosyncrasies, this drug will rarely cause irritative symptoms, if sufficiently diluted.

[11] It is scarcely necessary to state that there have been several cases of compound fracture of the skull in which death was due to hemorrhage or cerebral injury; such cases, however, are not included in the series mentioned above.

[12] It is of interest to note that there was no serious lesion of the kidneys in this case and that the hematuria was due entirely to an hemorrhagic cystitis.

Date.	Amount of hexamethylenamin given during 24 hours.	Method of administration.	Amount of liquids given during 24 hours.	Urine.	Highest temperature during day.
1910 June 13	135 grs.	By rectum.	250 cc. salt solution.	Normal.	105° F.
June 14	156 grs.	40 grains by rectum. 116 grains by mouth.	In 400 cc. salt solution. In 782 cc. (water, milk and broth).	Normal.	103.8° F.
June 15	90 grs.	60 grains by rectum. 30 grains by mouth.	In 300 cc. salt solution In 1050 cc. (water and nourishment).	Trace of albumen and a few red blood cells.	106° F.
June 16	.....	.....	500 cc. salt solution. 1290 cc. water and nourishment.	Trace of albumen and a few red blood cells.	104° F.
June 17	100 grs.	40 grains by rectum. 60 grains by rectum.	In 200 cc. salt solution. In 300 cc. salt solution.	Marked hematuria. Albumen and casts.	103° F.
June 18	.....	.....	1860 cc. by mouth.	Hematuria less marked.	102° F.
June 19	38 grs.	2 grains in every oz. of liquid by mouth.	1710 cc. by mouth.	Urine clear.	101.4° F.
June 20	81 grs.	2 grains in every oz. of liquid by mouth.	1800 cc. by mouth and by rectum.	Urine clear.	101° F.
June 21	68 grs.	1 grain in every oz. of liquid by mouth.	1650 cc. by mouth and by rectum.	Urine clear.	100.6° F.
June 22	41 grs.	1 grain in every oz. of liquid by mouth.	1410 cc. by rectum.	Urine clear.	100° F.

June 23d to July 4th from 15 to 30 grains of hexamethylenamin were given each day. The urine remained clear, and the patient was discharged apparently normal in every way; also was perfectly well when seen one year later.

HYPOPHYSIS CASES.

During the past three years there have been forty cases of hypophysis tumor, in the Johns Hopkins Hospital, in which the neighborhood symptoms were sufficiently marked to warrant an operative interference. The operation, as described by Dr. Cushing,[13] consists in the removal of the floor of the sella turcica, by an approach through the nose and sphenoid sinus, and incision of the dural covering of the gland, in order to relieve local pressure symptoms. In each case hexamethylenamin has been administered as a prophylactic measure; from 40 to 60 grains are given during the twenty-four hours preceding the operation, and even larger amounts for several days after the operation.

In thirty-one cases there were no post-operative complications whatever; in nine cases there was an escape of cerebro-spinal fluid through the nose for several days following the operation, together with an elevation of temperature, headache, slight stiffness of the neck and other symptoms suggesting a meningeal infection. Three of these cases finally succumbed with meningitis; the other six cases, however, recovered. The post mortem examination of the fatal cases showed that the operation had been misdirected and the cranial cavity entered anterior to the chiasm, directly inoculating the cortex with organisms from the mouth and nose.

[13] Cushing: The Pituitary Body, J. B. Lippincott Co., 1912. (To appear shortly.)

CEREBRO-SPINAL FISTULÆ.

The constant discharge of cerebro-spinal fluid into the nasal cavity, or middle ear, is not an infrequent complication of a cranial fracture, and usually leads to a fatal outcome from a secondary meningitis. Also, following certain operative procedures for the relief of increased intracranial pressure, the fluid may find its way out, even through the most carefully closed wound, and form a fistula, which is a great source of danger and is often extremely difficult to remedy. Such a condition necessitates a frequent renewal of dressings, and though every precaution may be taken, the cerebro-spinal space ultimately becomes infected with skin organisms.

In such conditions hexamethylenamin has proven of great value as a protection against meningeal infection. Our original observation on the excretion of this drug in the spinal fluid was made on a patient in whom a fistula had developed after an operation for a cerebellar tumor; and although at the time when the drug was first given there was an elevation of temperature, rigidity of the neck and many pus cells and bacteria of various kinds in the fluid escaping through the fistula, the patient began to improve and ultimately made a complete recovery. We have subsequently had six cases in which there was a similar condition, and all have escaped a fatal meningeal infection.

Since it is possible, in many cases of this character, to collect a specimen of the spinal fluid for chemical and bacteriological tests, one can accurately determine the size of the dose and the frequency with which the drug should be given in order to render this fluid an unsuitable culture media. It has been our custom to give the drug in small doses at intervals of thirty minutes or one hour, rather than the larger doses at four or six hour periods, as is usually recommended. In this way the drug is well diluted and toxic symptoms are less likely to be produced by large doses. When given at frequent intervals the drug is constantly present in the cerebro-spinal fluid, as may be shown by chemical tests, and the concentration at *all* times is sufficiently great to exert an inhibiting influence on the growth of the infecting organisms.

INFECTIONS OF THE EAR.

An infection of the middle ear is always attended with danger; a cerebral or cerebellar abscess, thrombosis of the lateral sinus, or an extension to the labyrinth, with a secondary meningitis, are not infrequent complications. When such complications do arise, the outcome is usually fatal, since it requires training of a very special nature in order to be able to recognize the condition during the early stages, and to carry out the surgical procedure indicated. It is, therefore, of the greatest importance that all infections of the middle ear be considered serious, and from the onset every precaution taken to discourage an extension of the infectious process.

Since Barton and others have shown that hexamethylenamin is excreted by the mucous membrane of the middle ear, and when given in large doses tends to discourage the local infection, the administration of this drug is doubly indicated in cases of otitis media. Although we have not had an extensive

series of such cases, we have, however, repeatedly seen a diminution in the amount and a change in the character of the discharge follow the administration of hexamethylenamin.

In two cases hexamethylenamin has apparently checked the progress of an acute labyrinthine infection; the following case is given as an example:

Surgical No. 27692. E. M., age 34, was admitted to the Johns Hopkins Hospital on April 24, 1911. For two weeks there had been a profuse, purulent discharge from the left ear, which had suddenly ceased thirty-six hours before admission. When admitted to the hospital, the patient was unable to sit erect or stand on account of dizziness. There was extreme tenderness over the left suboccipital region, but none over the mastoid itself; the temperature was 100.5° F., leucocytes 19,000; complained of diplopia; and there was a definite low grade of choked disc. Most striking was the constant rotary nystagmus to the left, which, however, could be stopped and reversed by irrigating the external auditory canal on the left with cold water. Bone and air conduction were both absent on the left side, but normal on the right. The drum on the left was hyperæmic and tense.

The patient was immediately given 60 grains of hexamethylenamin, and thereafter 100 grains each day until the subsidence of the acute symptoms. Although the drum was not punctured at this time, the relief was almost immediate. The headache, vertigo, nausea and vomiting had all ceased within two days after the drug was first administered, and the patient was discharged, apparently well, on May 4, 1911.

Dr. Cushing has recently seen in consultation a similar case, in which the headache, vertigo and symptoms of meningeal irritation rapidly disappeared, after giving large doses of hexamethylenamin.

Infections of the Nose.

It has also been shown that this drug is excreted by the mucous membrane of the accessory nasal sinuses, and its administration during the early stages of an ordinary "cold" will probably prove of value in preventing the chronic infections of these cavities.

Poliomyelitis.

The observations of Landsteiner and Popper,[14] and Flexner and Lewis[15] on the transmission of poliomyelitis to monkeys have demonstrated, among other things, that in the earliest stages of this disease there is leptomeningitis preceding the involvement of the central nervous system proper. This fact is of the greatest importance and at once suggests the possibility that hexamethylenamin might be of value in this disease. This supposition was confirmed, to a certain extent, in 1911, by the experimental studies of Flexner and Clark.[16] These authors ascertained that when the virus of poliomyelitis is injected intracerebrally in monkeys, in whom hexamethylenamin is already present in the spinal fluid, and the drug is then administered by mouth daily thereafter, that in many of the animals so treated, first, the incubation period of the disease is prolonged (from six to eight to twenty-four days), and, next, the onset of paralysis is entirely prevented.

These experimental observations are of the greatest significance since they indicate that protection may be afforded during the prevalence of an epidemic by the administration of hexamethylenamin, and furthermore, that the paralysis may be prevented by giving this drug during the earliest stages of the disease.

For the past two years the Massachusetts State Board of Health has recommended that hexamethylenamin be given, both as a therapeutic and as a prophylactic measure, during the prevalence of an epidemic; and numerous cases have been reported in which the recovery without paralysis was ascribed to the hexamethylenamin therapy. Skoog,[17] for example, in 1910, reports five cases in which the disease was recognized and hexamethylenamin treatment given during the prodromal stage; three recovered without paralysis; one developed paralysis, and another, "cared for under unfavorable circumstances," died.

Realizing, however, that a large number of cases must be studied in order to arrive at any definite conclusion concerning the value of hexamethylenamin in poliomyelitis, the writer, at the suggestion of Professor Goldmann and Professor Paul Erlich, visited Denmark and Sweden in the summer of 1911, at which time there was an extensive epidemic throughout entire Scandinavia. Through the kindness of Dr. Madsen, of Copenhagen, and Drs. Hellström and Arnold Josefson, of Stockholm, the writer was enabled to visit the larger of the infectious hospitals and institute hexamethylenamin treatment in all patients admitted during the preparalytic stage of the disease. The Health Department in Stockholm also consented to enforce the administration of hexamethylenamin, for a period of two weeks, to persons known to have been exposed to infection.

Dr. Arnold Josefson, of Stockholm, kindly undertook to personally examine the cases and supervise the treatment. As yet a sufficient number of observations have not been made to warrant any definite statements in regard to the value of this measure; Dr. Josefson,[18] however, in a brief report, in September, 1911, states, that of the first thirty cases, in which hexamethylenamin therapy was instituted, six were treated from the second day of the disease; one from the first day; and one from the third day. Each of these eight cases recovered without paralysis. He has also seen many cases in a more advanced stage of the disease, with facial or abducens palsy, in which the further progress of the disease was apparently checked by the administration of large doses of hexamethylenamin.

Since poliomyelitis is endemic in Norway and Sweden, it is hoped that we may soon be able to publish observations on an extensive series of cases.

Since the publication of our original reports in 1908-1909, others have made use of this measure for certain groups of cases.

[14] Landsteiner and Popper: Ztschr. f. Immunitätsforsch. u. exper. Therap., 1909, II, I Teil, 377-390.

[15] Flexner and Lewis: J. Am. M. Ass., 1909, LIII, 1639.

[16] Flexner and Clark: J. Am. M. Ass., 1911, LVI, 585.

[17] Skoog: J. Am. M. Ass., 1910, LV, 1804.

[18] Josefson: Allm. Svensk. Läkartidn., 1911, No. 41. Hygiea, 1911, LXXIII.

Barton,[19] in 1910, experimentally demonstrated that hexamethylenamin is excreted by the mucous membrane of the middle ear; and in seven cases of suppurative otitis media he found that the administration of this drug was promptly followed by a disappearance of the infecting organisms and a cessation of the discharge. In a recent analysis of 9590 cases of scarlet fever Holmgren[20] finds that there was a complicating otitis media in over 21 per cent, the majority of the cases occurring in children under five years of age. Barton, however refers to a long series of scarlet-fever cases in which hexamethylenamin was given as a prophylactic measure, and comments on the notable absence of middle ear infections in the cases so treated. At any rate, since it has been shown that hexamethylenamin is excreted into the middle ear, and in amounts which suffice to cause the rapid disappearance of the infecting organism, it would seem advisable that this drug be given, as a prophylactic measure, to every case in which a middle ear infection is a possible or threatened complication.

Barton, Brown,[21] and others, in 1910, called attention to the fact that hexamethylenamin is also eliminated by the mucous membrane of the para-nasal sinuses; and clinically these authors have found this drug of value in the treatment of acute and chronic sinus infections. Dr. Brown, himself, was suffering from a chronic suppuration of the right antrum of many years duration; within forty-eight hours after he began taking hexamethylenamin, however, there was a marked improvement in the local condition, and six days later the discharge had practically ceased.

Armstrong and Goodman,[22] in 1911, found that hexamethylenamin is eliminated by diseased bronchial or pulmonary tissue. In twelve cases in which hexamethylenamin was given, including pulmonary tuberculosis, pneumonia, bronchitis and asthma, the sputum in each instance was found to contain formaldehyde. Vanderhoof[23] has recently reported a series of cases of bronchitis in which the administration of hexamethylenamin has apparently been of decided therapeutic value.

There have been numerous publications during the past two years recommending that large doses of hexamethylenamin be employed in the treatment of ordinary colds, tonsillitis and other nose and throat infections. Our own experience has led us to believe that this drug is often of the greatest value in aborting an acute coryza, provided it be given in large doses and during the earliest stages of the infection.

Gradle,[24] in 1911, and more recently Ziegler, and others, have found that hexamethylenamin is excreted into the anterior chamber of the eye, and is of value in the treatment of various ophthalmic infections.

In regard to the use of hexamethylenamin in the prevention and treatment of meningeal infections, many interesting observations have been made by Stockmeyer,[25] Brem,[26] Ibrahim,[27] Rowell[28] and Hald.[l.c.]

Stockmeyer, in 1911, reported two cases of epidemic cerebro-spinal meningitis, which are of exceptional interest in this connection; the onset occurred practically simultaneously and in both cases the meningococcus could be demonstrated in smears and cultures.

Case No. I was given large doses of hexamethylenamin as soon as the character of the disease was recognized; in Case No. II, no hexamethylenamin was given, but otherwise the treatment was identical. When first seen both patients were unconscious, temperature 39.8° and 40.4° C., with Cheyne-Stokes respiration and a marked retraction of the neck. The case receiving hexamethylenamin immediately began to show improvement, while the second case steadily grew worse and succumbed on the fifth day. Owing to the appearance of a few red blood cells in the urine, the drug was discontinued, with an immediate return of coma, rigidity and irregular respiration. Large doses were again administered at two hour intervals, and again the patient immediately began to improve; on three occasions, subsequently, the drug was discontinued and each time the clinical condition would rapidly become worse. At the time of the report, six weeks after the onset of the disease, the patient had apparently made a complete recovery, with the exception of "a slight weakness of the feet."

We have had similar experiences with this drug in the treatment of experimentally produced meningitis in animals, and in two clinical cases with a meningeal infection; also it is well known that chronic infections of the bladder or kidneys may temporarily subside during the period of active therapy, but tend to reappear as soon as the hexamethylenamin is withdrawn.

The case described by Brem is of interest, since careful studies were made in order to determine the concentration of the drug in the cerebrospinal fluid, and its influence on the cell count and number of the infecting organisms. In this case, clearly one of meningococcus meningitis, hexamethylenamin was not given until the fourth day of the disease; it was then given in doses of 15 grains, and later increased to 20 grains, four times daily. Although there was no marked change in the clinical symptoms following the administration of this drug, the colorimetric tests indicated that formaldehyde was present in the cerebro-spinal fluid in a concentration of about 1 : 50,000. The cells in the spinal fluid were diminished from 18,000 to 3000 and later to 990 in each cmm.; and the meningococci, which were present in stained specimens and in cultures before, could not be demonstrated after the drug was given.

The comparatively long duration (23 days) of this acute meningeal infection, together with the decrease in pressure, diminution in cell count, and disappearance of the meningococci from the spinal fluid, all tend to confirm our previous contention that hexamethylenamin is excreted into the cerebrospinal fluid, and if given at frequent intervals will render this fluid an unsuitable media for the growth of microörganisms.

[19] Barton: J. Am. M. Ass., 1910, LIV, 1940; Boston M. and S. J., 1910, CLXII, 896.

[20] Holmgren: Hygiea, Stockholm, 1911, LXXIV, 257.

[21] Brown: J. Am. M. Ass., 1910, LIV, 1308.

[22] Armstrong and Goodman: J. Am. M. Ass., 1911, LVI, 1553.

[23] Vanderhoof: J. Am. M. Ass., 1912, LVIII, 331.

[24] Gradle: Ophth. Rec., 1911, March.

[25] Stockmeyer: Allg. Wien. med. Ztg., 1910, LV, Nos. 4-5.

[26] Brem: N. Y. Med. J., 1910, XCII, 816.

[27] Ibrahim: Med. Klinik, 1910, VI, 1893.

[28] Rowell: J. Am. M. Ass., 1909, LIII, 1641.

It may again be emphasized, however, that the chief value of hexamethylenamin lies in its use as a prophylactic measure.

Hald (*l. c.*), in 1911, made a series of careful quantitative estimations in order to determine the concentration of hexamethylenamin in the cerebro-spinal fluid and blood-serum. The concentration of the drug in the spinal fluid, removed by lumbar puncture from forty-five minutes to one hour after giving the usual dose (1 gram for adults; 0.5 gram for children) varied from 1:16,000 to 1:20,000. In the majority of the cases the concentration in the blood-serum, removed at the same time, was from two to four times greater than that in the cerebro-spinal fluid.

Fiaschi, in 1908, made the interesting observation that if hexamethylenamin is given by mouth formaldehyde may soon afterward be demonstrated in the fluid contents of hydatid cysts. In the cases observed by Fiaschi[29] the cysts were either in the liver or omentum. No mention is made of the effect of the drug on the parasite.

Chauffard,[30] in 1910, relates in detail a number of cases in which an acute cholecystitis occurred during the course of typhoid fever, and gives temperature charts and other data showing the prompt relief which followed the administration of hexamethylenamin.

Riddle,[31] in 1911, published the results of some studies made on fowls; he found that when hexamethylenamin is fed to laying hens, this drug passes through the follicular and vitelline membranes and is deposited in the egg, where it undergoes decomposition, liberating free formaldehyde. Moreover, he found that the eggs from fowls receiving hexamethylenamin contain a sufficient amount of formaldehyde to act as a preservative; such eggs remain fresh and palatable for a much longer period than do the control eggs from untreated hens. Sodium salicylate and sodium benzoate, when fed to hens, cannot be detected in the eggs.

Toxic Symptoms.

Although hexamethylenamin, or its modifications, has been in common use for the past fifteen years, there are but very few reports in which serious toxic symptoms are ascribed to this drug. In 1894, Nicolaier called attention to the fact that some individuals seem to be especially susceptible to hexamethylenamin, and even when administered in small amounts (5 to 7½ grains) painful micturition and hematuria may result. In the experimental production of hematuria, however, this author found it necessary to give as much as 230 grains a day, for several days, to a dog weighing twenty kilos; and even then, after the subsidence of the acute symptoms, microscopic examination of the kidneys failed to disclose any evidence of permanent damage. Nicolaier has also given patients, suffering with acute infections of the genito-urinary tract, as much as 150 grains at a single dose, without ill effect.

Maguire,[32] experimenting upon himself, injected 100 cc. of a 1:2000 solution of formaldehyde intravenously, and one hour later the urine was found to contain albumen; 263 cc. of a 1:2000 solution produced hematuria with blood clots, which entirely disappeared, however, within twenty-four hours; a third injection of 63 cc. of a 1:1000 formaldehyde solution was followed by sharp abdominal pains, diarrhœa, hematuria, and catarrh of all the mucous membranes. Ewing, Park, and Payne got like results from the injection of formalin in rabbits.

More recently, Frothingham,[33] studying the effect of the subcutaneous administration of hexamethylenamin on guinea pigs, found that from 7½ to 75 grains can be injected under the skin in these small animals without producing any apparent organic lesion. In some instances there was a local reaction and necrosis at the site of the injection.

Of 486 cases of typhoid fever in the Massachusetts General Hospital, referred to by Easton,[34] nearly all received from 8 to 10 and some 15 grains of hexamethylenamin three times a day, for a period of two to three weeks; there were three cases of painful micturition and two of hematuria. The symptoms in each of these cases rapidly disappeared after withdrawing the drug, and left no evidence of permanent damage.

In our experience there have been but very few instances in which toxic symptoms have resulted from the administration of large doses of hexamethylenamin, although we have repeatedly given from 200 to 300 grains daily for four or five days; even in children, doses of 100 or 125 grains a day, have produced no irritative symptoms, provided it was possible to administer the drug sufficiently diluted with water. We have abandoned the custom of giving this drug in doses of 10 or 15 grains at stated intervals, since it is often difficult to induce the patient to take, at one time, the 250 or 300 cc. of water in which doses of this amount should always be dissolved. In case the patient is very ill, the drug is usually administered per rectum, from 50 to 100 grains being dissolved in a liter of salt solution and allowed to slowly flow into the bowel, a drop at a time. In no case has there been the slightest evidence of undue irritation of the intestinal mucosa, when the drug is thus given, and as a rule the salt solutions are well absorbed, even after one or two weeks of almost continuous administration by this method. If the patient is able to take nourishment by mouth, from 2 to 3 grains of hexamethylenamin are added to every ounce of liquid, since the drug is practically tasteless, and it is often possible, in this way, to give from 60 to 100 grains a day without the patient's knowledge and without producing gastric or renal irritation.

In 95 of our cases in which the average dose of hexamethylenamin was 75 grains a day for ten days, painful micturition and hematuria occurred in seven instances. Two of these cases were fatal meningeal infections of otitic origin; the patients were desperately ill when brought to the hospital, and the drug was given in unusually large amounts, with the hope of checking the progress of the infection. A third was a case of tuber-

[29] Fiaschi: Austral. M. Gaz., 1908, XXVII, 394; (also personal communications).

[30] Chauffard: Semaine méd., Paris, 1911, XXXI, 109.

[31] Riddle: Science, U. S., 1911, XXXIV, 887-889.

[32] Maguire: Lancet, 1900, II, 1709-1714.

[33] Frothingham: Arch. Internat. Med., 1909, IV, 510-515.

[34] Easton: Boston M. and S. J., 1905, CLIII, 195.

culous meningitis in a child seven years of age. In each of these cases there was a well marked hematuria, but at the post mortem examination it was apparent that it had its origin from the mucous membrane of the bladder and was not due to an acute renal irritation. In the remaining four cases the urine rapidly became normal on the withdrawal of the drug.

Although there are undoubtedly certain individuals who have a personal idiosyncrasy for hexamethylenamin, and even a small dose may cause uncomfortable symptoms—such as a skin rash, catarrh of the mucous membranes, gastric or urinary irritation—this fact does not invalidate the use of the drug. Aside from personal idiosyncrasies our experience has been that untoward symptoms usually arise as a result of insufficient dilution, and such symptoms have invariably disappeared on withdrawing the drug and producing active diuresis by forcing liquids.

THE EFFECT OF JAUNDICE, PRODUCED BY LIGATION OF THE DUCTUS CHOLEDOCHUS, UPON THE PANCREATIC SECRETION.

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We know very little about the quantitative and qualitative changes in the pancreatic secretion due to organic or functional disturbances. Even experimental knowledge of the pancreas is so far from complete that any contribution to the subject seems worthy of being chronicled.

The object of our series of experiments was to determine the effect of jaundice, produced by ligating the *ductus choledochus*, upon the amount of pancreatic juice, its rate of flow and its ferment-content. The method employed was first making a pancreatic fistula and studying the secretion from this with the different types of food, meat, milk, and bread; then performing a second operation, the ligation of the gall-duct, and again, after studying the pancreatic secretion after the same kinds of foods, comparing the two and drawing certain conclusions as to the influence of jaundice so produced upon this secretion. As is well known, the pancreas has two or three ducts, and in the Pawlow method used by us, the lowest of these was the one ligated. As Pawlow and Bickel and their students have shown, this secretion may be produced by the sight or smell of food, and may be inhibited or entirely stopped by various reflex nervous influences such as excitement, anger, the sexual feeling, etc., although, mainly through the work of Bayliss and Starling, we know that chemical influences, acting as a secretin, play the most important rôle in calling forth this secretion. The pancreatic secretion, especially the trypsinogen, must be activated by the enterokinase of the intestinal mucous membrane; usually there is enough mucous membrane about the mouth of the pancreatic duct in the Pawlow operation to furnish this activating agent, and it is rarely necessary to add intestinal juice from another animal. Probably in this necessity for activation by the enterokinase lies the reason for the absence of the pancreatic auto-digestion *intra vitam*. It must not be forgotten that certain substances besides enterokinase can activate the pancreatic juice, notably the soluble calcium salts (Abderhalden), while other substances, such as pus, may produce a markedly inhibitory effect.

The quantitative study of the pancreatic secretion shows that it varies markedly with the different foods, carbohydrate food furnishing the most juice, fat the least, while as a rule the richness in ferment is in inverse proportion to the quantity of juice; most investigators have noted a close correspondence of the quantity of bile to that of pancreatic juice secreted, although, according to Pawlow, fat stands between carbohydrate and proteid in its bile-forming power. As to the bile secretion, although markedly increased by the taking of food and by bile-absorption in the intestines, it is nevertheless in part independent of the processes in the digestive tract; in other words, there are substances constantly circulating in the blood which can stimulate the metabolic activity of the liver-cells and possibly, though this must be to a comparatively slight extent, there is a secretion arising through nervous influences (Fleig); the flow of the bile from the gall-bladder into the intestine depends on various influences originating reflexly from the duodenal mucous membrane. The activating power of the bile upon the pancreatic juice, especially upon its lipase, and its aid in fat absorption, must not be forgotten. When considering the effects of icterus, we must think of (1) those due to lack of bile in the intestine manifesting themselves in digestive disturbances, (2) those due to the bile circulating in the blood, especially the action of the cholates upon the nervous tissues, and (3) the disturbances produced in the liver-cells by the action of the concentrated bile under increased pressure. In the sudden death of the dogs in both our experiments these factors must be taken into consideration, especially the toxic effect of the cholates, although in all probability the stormiest and most severe nervous symptoms are due more to the harm done to the vital processes in the liver-cells, than to the direct action of the absorbed bile-constituents upon the nervous tissues. Von Reuss showed that ligation of the gall-duct in dogs produced a diminution of glycogen in the liver, and in rabbits markedly lessened the glycosuria after the Claude Bernard sugar-puncture, while Glube (Med. Klinik., 1911, No. 43) from

thirteen experiments on two dogs concluded that after ligation of the gall-duct the curve of secretion of the pepsin was reversed, and not only was the percentage of pepsin in the juice diminished, but also the absolute amount.

Although, clinically, we recognize that jaundice produces marked disturbances in the intestinal as well as in the gastric digestion, the cases in which this can be studied quantitatively are extremely few in number, while even along experimental lines, comparatively little has been done. In man, conclusions regarding the effect of various conditions upon the pancreatic secretion must be made from the rare, post-operative pancreatic fistulas, from the examination of the urine and fæces for the pancreatic ferments, from pancreatic juice obtained from the stomach after administering olive oil or from the duodenum itself by especially devised instruments, from the examination of the stools for fat or undigested nuclei, or of the urine for sugar and for the Cammidge reaction. None of these, however, has furnished very definite results, and so we are obliged to place much reliance upon animal experiments; but we must not forget, in their interpretation, that it is unjustifiable to assume that the conditions are the same in man as in animals, although probably in many respects they are.

Our experiments, eighteen in number upon two dogs, were carried out as follows: The dogs were operated upon under ether anæsthesia, and with the most careful aseptic technique; the lowest pancreatic duct, with a small area of mucous membrane surrounding its mouth, was separated from the intestine, and sewed into a small opening made in the abdominal wall; the intestinal wound and the abdominal incision were closed. Healing was perfect in the case of the first dog, but there was a slight infection about the mouth of the duct in the second. Three or four days after the operation, the dogs were in condition to be studied. After 24 hours fasting, milk, meat or bread in measured amounts were given, and the resultant pancreatic secretion carefully collected and measured. In the mixed specimen of every two hours, the trypsin and the diastase were quantitatively estimated, the experiment lasting for six hours after the feeding. Generally, a day or more under normal mixed diet was allowed to intervene before the succeeding experiment was made.

In the case of the *first dog,* three preliminary experiments were made with 150 ccm. milk, three with 150 grams lean, fat-free beef, and two with 150 grams bread, while in the case of the *second dog,* three preliminary experiments were made with 500 ccm. milk, and two with 150 grams lean beef. From these experiments we could obtain average figures for quantity, trypsin and diastase after milk, meat and, in the case of the first dog, bread for six hours after feeding; these figures will be found in the tables at the end of the article, and are expressed graphically in the subjoined curves.

The dogs were then operated upon the second time—ether anæsthesia and the same careful technique, of course, being employed; a double ligation of the *ductus choledochus* was made and the duct cut between the two ligatures so as to insure a complete absence of bile from the intestines. Two days later the dogs were in excellent condition and had entirely recovered from the immediate effects of the operation; experiments were then carried on as before in regard to the pancreatic secretion, although it was impossible to get either dog to take bread. In subsequent experiments, we hope by the use of soft carbohydrate foods, in soup or purée form, which may be given through the stomach tube, to obtain figures also after carbohydrate feeding. In the case of the first dog the experiment was carried on as before the ligation of the gall-duct, that is, the food was given to the dog after fasting 24 hours, and a day of feeding with mixed diet intervened before the next experiment, but the second dog was fed immediately after the experiment with one pound of horse flesh, and the next experiment begun the following morning. In the case of the *first dog,* one experiment with 150 ccm. milk, one with 150 grams lean meat, and one with no food were carried out, no further experiments being possible, as after the removal of the bile from the intestine death occurred in 7 days, while with the *second dog,* one experiment was made with 500 ccm. milk, and one with 150 grams lean meat, death occurring four and one-half days after operation. In each case the dog recovered rapidly from the immediate effects of this second operation, remained quite well for five days in the case of the first dog, and three days in the case of the second, and from then on lost weight and strength with great rapidity. The *autopsy* of the *first dog* showed that both operations were perfect, there was no peritonitis, the liver was enlarged, all the organs were very yellow, and the gall-duct was much distended, while, histologically, some pus-cells and red blood corpuscles were seen in the larger pancreatic duct. In the *second dog* there was no peritonitis, the liver was only slightly enlarged, all the organs were bile-stained, and there was about 500 ccm. of fluid apparently almost pure bile, in the peritoneal cavity as the proximal ligature had slipped from the gall-duct. This may have accounted for the slight difference in the two cases, and the earlier death of the second dog, as here obviously there was a far greater opportunity for the rapid absorption of bile into the general circulation.

In our experiments the diastase was determined quantitatively by Wohlgemuth's method. Five cubic centimeters of a one per cent soluble starch solution were added to each of a row of test-tubes to which pancreatic juice in decreasing amounts had been added, 0.5 ccm. in the first tube, 0.25 ccm. in the second, 0.125 in the third, etc.; the tubes were kept in the water-bath at a temperature of 37.5°-39°C. for a half hour, and after being cooled and having been almost filled with water, were tested with a drop or two of decinormal iodine solution. The diastatic units are the number of cubic centimeters of a one per cent starch solution which should be entirely digested in one-half hour by 1 ccm. of pure pancreatic juice. The trypsin was determined by the casein method, 2 ccm. of a one per

cent casein solution being in each tube with decreasing amounts of pancreatic juice, the tubes being kept in the water-bath for one hour, and then tested with acetic alcohol (acetic acid 1 ccm., alcohol 45 ccm., distilled water to 100 ccm.). The trypsin units, in other words the tryptic strength of the juice, are the number of cubic centimeters of a one per cent casein solution which would be completely digested by 1 ccm. of pure juice in one hour.

A survey of the accompanying figures and diagrams will show the results of our experiments, which in the main follow the law that the less the amount of juice the greater its richness in ferment and vice versa. The differences in the figures in the experiments with the same amounts of the same food, *e. g.*, milk, can probably be explained partly at least on psychical grounds, appetite, surrounding sights and sounds, etc. In the main, however, the figures in the individual experiments with the same foods harmonize quite closely, and the average figures for quantity, trypsin and diastase, may be regarded as fairly typical of the effect of the various foods on the quantity of juice and its ferment-richness. We, of course, are speaking now of the results of the experiments *before* the performing of the second operation. The antitryptic action of the pus probably explains the fact that no trypsin could be demonstrated in the first two experiments with the second dog, as even the addition of pure intestinal juice (enterokinase) from another dog failed to bring about digestion of the casein; with the disappearance of the pus from about the mouth of the pancreatic duct, the tryptic action of the juice became manifest, but always to a less extent than in the case of the first dog.

When we study, however, the figures after the ligation of the gall-duct, in other words, try to determine the effect of rapidly developing jaundice due to the complete occlusion of the duct upon the pancreatic secretion, we note at once that this is very marked—more juice being secreted now after milk than after meat, while the richness of the juice in diastase and trypsin was also, broadly speaking, practically reversed. The diagrams show this especially well. The first dog was especially interesting in that up to an hour before death, even although fasting, there was a constant flow of pancreatic juice averaging 6.4 ccm. per hour with 1280 diastase units and 4096 trypsin units in each cubic centimeter; this may have been due to stimulation of the pancreas by the circulating bile-stuffs.

In both cases death was sudden, although for the preceding 24 to 48 hours there had been a rapid loss of weight and strength; this sudden death may be accounted for by the loss of such a great amount of alkali, by disturbances in fat metabolism, by the effects of the circulating bile-stuffs upon the body, especially of the cholates upon the nervous tissues, or by changes produced in the liver cells by the action of the concentrated bile under increased pressure, thus possibly allowing toxins from the intestinal canal to reach the general circulation. The extremely good condition of each dog after the first operation would seem to show that the bile and intestinal juice can act vicariously in the absence or marked diminution of the pancreatic secretion, and that it is only after the shutting off of the bile, in addition, that processes develop which lead to death in such a short time.

From this series of experiments we may, we believe, draw the following conclusions:

1. After the ligation of the gall-duct and the consequent production of a rapidly developing jaundice there is a marked reversal in the pancreatic juice both as regards amount and ferment-richness after the different types of foods: there is more juice with milk than with meat, and where before, the trypsin or the diastase showed a definite increase, now a decrease would be likely to be met with and vice versa.

2. The removal of the bile from the intestine after the previous withdrawal of the major portion of the pancreatic secretion produces in a very short time a rapid loss of weight and strength, ending in sudden death, and emphasizes anew the great importance of the bile as a partial substitute for the pancreatic secretion if the latter is absent or markedly diminished.

Detailed figures of all the experiments and graphic representations of certain of these figures follow.

Dog A.—Operation for Pancreatic Fistula (Pawlow), Oct. 25, 1911. Preliminary study of the pancreatic secretion.

Day.	Food.	Hour.	Amount of Juice.	Diastase in Starch Units.	Trypsin in Casein Units.
Experiment 1:					
Oct. 30.	Milk, 150 ccm.	1	1.8 ccm.	5120	128
		2	2.5 ccm.		
		3	3.8 ccm.	2560	512
		4	1.6 ccm.		
		5	4.2 ccm.	5120	1024
		6	2.0 ccm.		
		Total,	15.9 ccm.		
Experiment 2:					
Nov. 1.	Milk, 150 ccm.	1	1.4 ccm.	640	2048
		2	.9 ccm.		
		3	.7 ccm.	320	4096
		4	1.0 ccm.		
		5	1.9 ccm.	1280	4096
		6	1.9 ccm.		
		Total,	7.8 ccm.		
Experiment 3:					
Nov. 3.	Milk, 150 ccm.	1	.7 ccm.	1280	....
		2	1.2 ccm.		
		3	1.6 ccm.	1280	....
		4	3.2 ccm.		
		5	4.4 ccm.	1280	....
		6	7.8 ccm.		
		Total,	18.9 ccm.		
Experiment 4:					
Nov. 6.	Meat, 150 grams.	1	44.8 ccm.	1280	8192
		2	46.2 ccm.		
		3	48.2 ccm.	1280	1024
		4	25.8 ccm.		
		5	8.8 ccm.	1280	2048
		6	8.2 ccm.		
		Total,	182.0 ccm.		

Day.	Food.	Hour.	Amount of Juice.	Diastase in Starch Units.	Trypsin in Casein Units.
Experiment 5:					
Nov. 8.	Meat, 150 grams.	1	23.5 ccm.	1280	....
		2	4.4 ccm.		
		3	8.2 ccm.	1280	....
		4	6.9 ccm.		
		5	2.9 ccm.	1280	....
		6	7.6 ccm.		
		Total,	53.5 ccm.		
Experiment 6:					
Nov. 10.	Meat, 150 grams.	1	7.0 ccm.	1280	256
		2	.8 ccm.		
		3	5.2 ccm.	640	512
		4	12.9 ccm.		
		5	4.8 ccm.	1280	1024
		6	20.1 ccm.		
		Total,	50.8 ccm.		
Experiment 7:					
Nov. 13.	Bread, 150 grams.	1	35.9 ccm.	1280	512
		2	28.0 ccm.		
		3	15.6 ccm.	1280	1024
		4	9.1 ccm.		
		5	7.3 ccm.	2560	2048
		6	8.4 ccm.		
		Total,	104.3 ccm.		
Experiment 8:					
Nov. 15.	Bread, 150 grams.	1	71.8 ccm.	1280	512
		2	45.0 ccm.		
		3	22.4 ccm.	1280	1024
		4	12.4 ccm.		
		5	8.2 ccm.	1280	2048
		6	6.4 ccm.		
		Total,	166.2 ccm.		
Average figures:					
	Milk, 150 ccm.	1	1.3 ccm.	2347	1088
		2	1.33 ccm.		
		3	2.03 ccm.	1387	2304
		4	1.93 ccm.		
		5	3.5 ccm.	2560	2560
		6	3.9 ccm.		
		Total,	14.19 ccm.		
	Meat, 150 grams.	1	25.1 ccm.	1280	4224
		2	17.0 ccm.		
		3	20.53 ccm.	1077	768
		4	15.2 ccm.		
		5	5.5 ccm.	1280	1536
		6	11.97 ccm.		
		Total,	95.3 ccm.		
	Bread, 150 grams.	1	53.85 ccm.	1280	512
		2	36.5 ccm.		
		3	19.0 ccm.	1280	1024
		4	10.25 ccm.		
		5	7.75 ccm.	1920	2048
		6	7.4 ccm.		
		Total,	134.75 ccm.		

Operation: Ligation of the gall-duct. Nov. 17, 1911.

Experiment 9:					
Nov. 20.	Milk, 150 grams.	1	10.4 ccm.	1280	512
		2	31.3 ccm.		
		3	7.6 ccm.	2560	2048
		4	6.6 ccm.		
		5	21.6 ccm.	1280	512
		6	8.8 ccm.		
		Total,	86.3 ccm.		
Experiment 10:					
Nov. 22.	Meat, 150 grams.	1	10.3 ccm.	1280	2048
		2	13.8 ccm.		
		3	10.8 ccm.	1280	2048
		4	10.6 ccm.		
		5	11.8 ccm.	1280	4096
		6	11.9 ccm.		
		Total,	69.2 ccm.		

Dog B.—Operation for Pancreatic Fistula (Pawlow), Nov. 28, 1911.
Preliminary study of the pancreatic secretion.

Day.	Food.	Hour.	Amount of Juice.	Diastase in Starch Units.	Trypsin in Casein Units.
Experiment 1:					
Dec. 4.	Milk, 500 ccm.	1	3.4 ccm.	640	....
		2	3.8 ccm.		
		3	2.6 ccm.	640	....
		4	3.1 ccm		
		5	4.9 ccm.	640	....
		6	2.5 ccm.		
		Total,	20.3 ccm.		
Experiment 2:					
Dec. 6.	Milk, 500 ccm.	1	2.2 ccm.	640	....
		2	5.9 ccm.		
		3	6.8 ccm.	640	....
		4	7.9 ccm.		
		5	7.2 ccm.	640	....
		6	11.4 ccm.		
		Total,	41.4 ccm.		
Experiment 3:					
Dec. 8.	Meat, 150 grams.	1	4.2 ccm.	640	128
		2	11.4 ccm.		
		3	13.7 ccm.	640	32
		4	14.2 ccm.		
		5	13.3 ccm.	640	64
		6	12.7 ccm.		
		Total,	69.5 ccm.		
Experiment 4:					
Dec. 11.	Meat, 150 grams.	1	14.1 ccm.	640	128
		2	10.5 ccm.		
		3	10.5 ccm.	640	256
		4	7.3 ccm.		
		5	3.3 ccm.	640	256
		6	1.7 ccm.		
		Total,	47.4 ccm.		
Experiment 5:					
Dec. 13.	Milk, 500 ccm.	1	1.4 ccm.	1280	512
		2	8.1 ccm.		
		3	8.8 ccm.	1280	256
		4	9.2 ccm.		
		5	4.9 ccm.	1280	512
		6	4.3 ccm.		
		Total,	36.7 ccm.		
Average figures:					
	Milk, 500 ccm.	1	2.3 ccm.	853	512
		2	5.9 ccm.		
		3	6.1 ccm.	853	256
		4	6.7 ccm.		
		5	5.7 ccm.	853	512
		6	6.1 ccm.		
		Total,	32.8 ccm.		
	Meat, 150 grams.	1	8.2 ccm.	640	128
		2	11.0 ccm.		
		3	12.1 ccm.	640	144
		4	10.7 ccm.		
		5	8.3 ccm.	640	160
		6	7.2 ccm.		
		Total,	57.5 ccm.		

Operation: Ligation of the gall-duct. Dec. 14, 1911.

Experiment 6:					
Dec. 15.	Milk, 500 ccm.	1	2.3 ccm.	1280	1024
		2	2.8 ccm.		
		3	2.6 ccm.	1280	2048
		4	2.6 ccm.		
		5	2.7 ccm.	1280	4096
		6	6.8 ccm.		
		Total,	19.8 ccm.		
Experiment 7:					
Dec. 16.	Meat, 150 grams.	1	.2 ccm.	1280	4096
		2	.2 ccm.		
		3	.2 ccm.	160	128
		4	.3 ccm.		
		5	.1 ccm.	160	128
		6	.0 ccm.		
		Total,	1.0 ccm.		

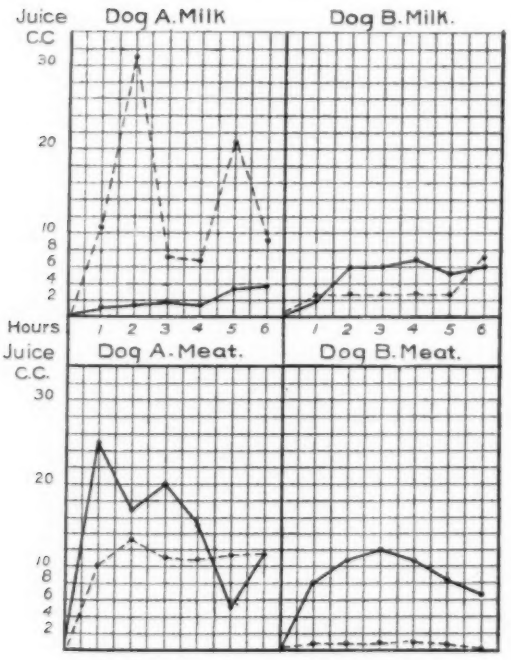
STUDIES ON THE EFFECT OF EXPERIMENTAL JAUNDICE ON THE PANCREATIC SECRETION.

AVERAGE CURVES.

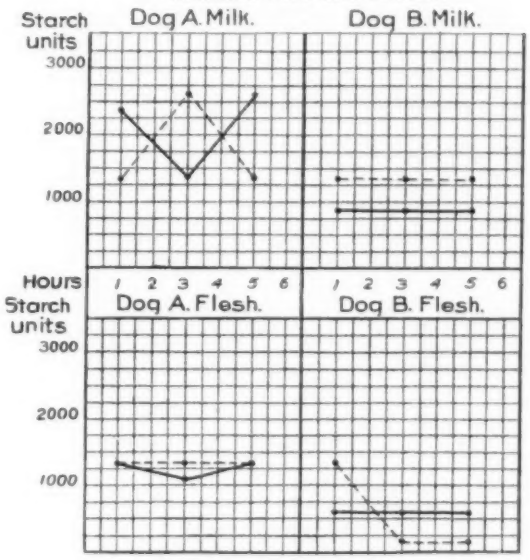
Quantity—curves with milk,
curves with meat.
Diastase—curves with milk,
curves with meat.
Trypsin—curves with milk,
curves with meat.

Before ligation of gall-duct ————
After ligation of gall-duct - - - - - -

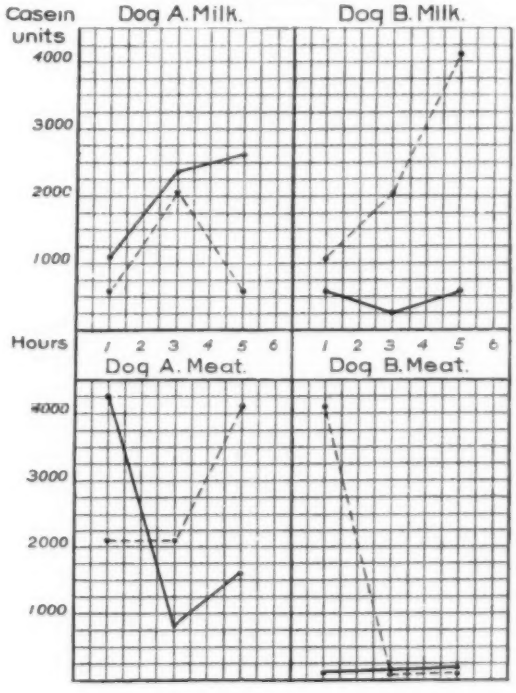
AVERAGE QUANTITY CURVES.



AVERAGE DIASTASE CURVES.



AVERAGE TRYPSIN CURVES.



JOHNS HOPKINS HOSPITAL BULLETIN.

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UNDESCENDED CŒCUM IN THE SUB-HEPATIC POSITION.

By Joseph Marshall Flint, M. D.

(From the Continuous Surgical Service of the New Haven Hospital and the Surgical Laboratory of Yale University.)

The importance of embryology in the interpretation of pathological conditions met at operations has frequently been emphasized. In fact, many pathological states have for their sole explanation the persistence of fœtal stages of development, where an arrest of the usual process of individual evolution has taken place. Many anomalies of the gastro-intestinal tract can be explained only on this basis as the following case shows. Although the embryonic condition maintained in this patient had no definite association with the disease which

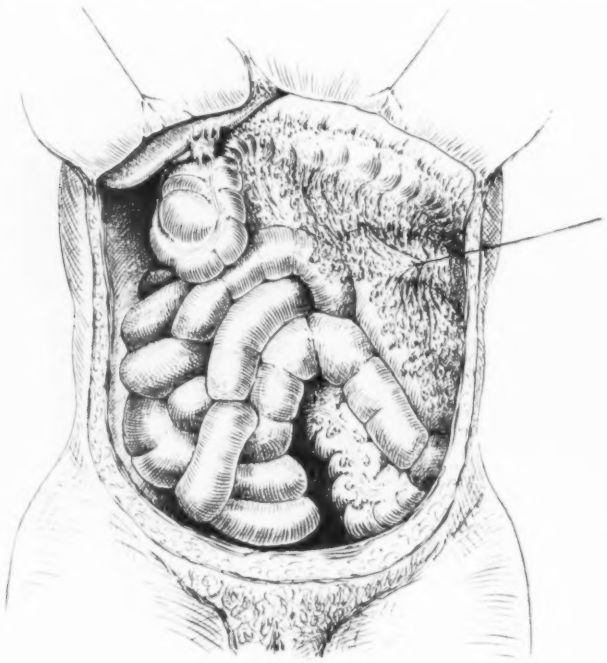

Fig. 1.

brought her to the operating table, it is nevertheless of great interest, for obviously a primary process beginning in the appendix would have led to great difficulties in diagnosis as in a case I saw some years ago in another clinic where an acute appendicitis gave a perfect clinical picture of an acute cholecystitis owing to adhesions between the tip of an abnormally long appendix and the fundus of the gall bladder.

The patient, Mrs. B., aged 38, has suffered for nine years from typical gall-stone colic with sharp attacks of pain at Robson's point which radiated to the costal margin and the right scapula. These attacks were of a sharp lancinating character and associated with vomiting, first of undigested food and then green slimy vomitus. The attacks have varied in frequency, but have averaged about every five or six months. Between attacks, she has suffered from indigestion chiefly in a feeling of fullness after eating and flatulence. She has never been jaundiced. Of late years, she has become accustomed to the pain and is never without a feeling of discomfort in the right hypochondrium. She has always been constipated, but recently the condition has become much worse. In other respects, she has been always quite well. Mrs. B. is the mother of five children and aside from the usual diseases of childhood, has had no other illnesses. She has never had typhoid fever.

The physical examination is in general negative except for a chronic parenchymatous nephritis. The liver is not enlarged. Over Robson's point there is distinct tenderness and muscle spasm on light palpation. Somewhat to the right, a small hard mass can be felt which is not sensitive to light pressure, but is painful on deep palpation. This mass is

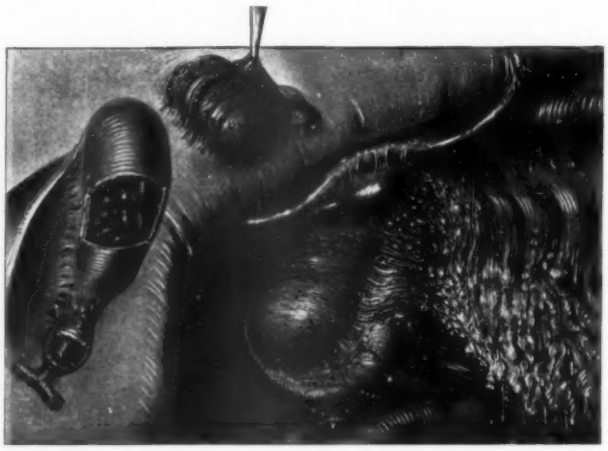

Fig. 2.

undoubtedly a thickened gall bladder. The remainder of the abdomen is negative.

The operation was carried out through a Kocher incision which revealed the conditions shown in Figs. 1 and 2. The cœcum lies just beneath the liver in the usual position of the hepatic flexure with an infantile type of appendix which lies under the cœcum and curls up so that its tip lies beside the fundus of the thickened and adherent gall bladder. Stretching over the cœcum is a thin veil which extends from its under surface and is continuous with the omentum. There was no ascending colon, the cœcum forming the right end of the transverse colon with which the omentum is fused in the usual manner. The gall bladder, much thickened and adherent to the cœcum, stomach, and duodenum, is filled with stones. A large stone lies impacted in the cystic duct. After separating the adhesions, a cholecystectomy was done in the usual manner. The appendix was also removed. The post-operative convalescence was uncomplicated. All drainage was removed on the thirteenth day and the patient discharged from the hospital on the twenty-fifth day with the wound entirely healed.

To understand the condition presented by this patient, it is necessary to recall the various stages in the development of the gastro-intestinal tract, from the simple straight tube with a ventral and dorsal mesentery extending as low as the level of the upper part of the duodenum and only a dorsal mesentery below that point. Where the increasing length of the lower segment carries it out into the umbilical cœlom, the primary rotation of the gut around the axis of the superior mesenteric artery occurs from the second to the third month, after which the intestine returns to the abdominal cavity. The rotation is completed within the abdomen and the cœcum takes the sub-hepatic position to the right side and just below the liver. Later, with the formation of the ascending colon, it descends into the right iliac fossa about the eighth month of fœtal life establishing conditions approximating those found in adult life.

At any of these fœtal stages, the process of development may be arrested or retarded yielding anomalous topographical relationships of the intestine. Instances have been recorded of failure of the intestine to rotate with a left-sided cœcum or the process may stop after rotation with the cœcum lying beneath the liver as in the instance recorded in this paper. On the other hand, the descent may be excessive and the cœcum become a pelvic organ.

Smith * has published an admirable review of the anatomical position of the cœcum based on observations made from a series of 1050 autopsies upon infants most of whom were under three months of age. From his paper, I quote the following table:

Position of Cœcum.	No. of cases.
Cœcum on left side without rotation of the intestine	5
Cœcum undescended in sub-hepatic position	63
Cœcum in right iliac fossa	882
Cœcum in pelvis	100
Total	1050

It will be seen that in the majority of cases, the cœcum is in the iliac fossa in what is considered its normal position. In 5 cases there was no rotation of the intestine, in 63 the condition presented by our case obtained, while in 100 the cœcum was found in the pelvis. There is, of course, an enormous difference between infantile and adult anatomy, making a large readjustment of the viscera necessary between the periods of infancy and maturity. Accordingly it is probable that many of these arrested, or, to describe them more accurately, delayed processes, are corrected before growth is completed as is shown so frequently in the late descent of an abdominal or inguinal testis. While the conditions shown in this table would not represent a fair average of 1000 similar autopsies on adults, it is of importance, however, to remember the possibilities of delayed or arrested development in the position of the viscera and the intestine.

It is apparent then that the condition presented by our patient is to be found in a state of arrested development of the intestine following the rotation of the gut leaving the cœcum in the sub-hepatic position. This usual descent of the cœcum with the formation of the ascending colon which occurs about the eighth month of intrauterine life failed to succeed the rotation and the cœcum was left, in consequence, in its fœtal position beneath the liver just adjacent to the gall bladder. In this instance, no ascending colon was present, so the cœcum formed simply a cul de sac on the hepatic end of the transverse colon occupying a position about the usual site of the hepatic flexure. Spreading over the cœcum was a typical membrane such as has been described by Jackson and variously termed Jackson's veil or membranous pericolitis. This membrane was continuous with the omentum and gradually and insensibly passed on from a typical veil into typical omentum as is shown in the illustration indicating the conditions found at operation. The importance of this feature of the case as affording a possible explanation of the origin of certain of these pericolic membranes, I shall discuss in a later paper. It is not impossible, however, that these membranes which are derived from the omentum or the secondary peritoneal fusions after the rotation of the intestine may be responsible for the failure of the cœcum to descend by fixing it permanently in the sub-hepatic position. For the moment I simply wish to emphasize this point and the interest of persistent embryological conditions in the pathology of the gastro-intestinal tract especially owing to the possible difficulties in diagnosis to which such misplacement may lead.

* Smith. Anatomical Record. Vol. 5. 1911.

THE PRESENT STATUS OF THE ANTI-TYPHOID CAMPAIGN IN GERMANY.*

By WILLIAM W. FORD, M. D., D. P. H.,

Associate Professor of Hygiene and Bacteriology, The Johns Hopkins University.

In that portion of the Rhine country where the Franco-German war was fought, now entirely controlled by Germany, before 1870 back to the days of Napoleon largely in the possession of the French, and previous to the Napoleonic campaigns the battleground of many a conflict between Teuton and Gaul, a fight has been waged against typhoid fever during the past decade which, to the well-trained medical man, is more full of interesting details than any of the collisions between the rival nations. To understand the motives which underlie this campaign we must consider for a moment the historical development of hygiene in Germany and picture to ourselves the con-

* Address delivered at the graduation exercises of the Naval Medical School, Washington, and before the Johns Hopkins Hospital Medical Society.

ditions in Alsace-Lorraine which led Robert Koch, in 1902, to inaugurate a new method of preventing the spread of typhoid fever.

Following the advice of the founder of modern hygiene, Max v. Pettenkofer, Professor of Hygiene in the University of Munich, and indeed the first professor of this subject in any German university, about the year 1870 the cities of central Europe began to adopt the measures which the wise Pettenkofer had advocated to control the diseases of the soil (the *Bodenkrankheiten*), Asiatic cholera, typhoid fever and dysentery. The city of Vienna, for instance, built within narrow walls, deriving its water supply from surface wells sunk in a sewage-permeated soil, had typhoid fever year in and year out. In the year 1874 a new supply of clean pure water was obtained from outside the city limits and within a year the typhoid mortality was cut in two, falling from 15-16 per cent to 7-8 per cent. The typhoid-infested Munich canalised its sewage system, washed these canals out with a branch of the river Isar, established a good supply of drinking water and eliminated the typhoid fever from its midst. Similar measures were equally effective in the other great cities of Germany, Berlin, Leipzig, Dresden and Frankfurt, freeing their population of this widespread scourge.

With the advent of the science of bacteriology and especially with the discovery of the cholera vibrio in 1883 by Robert Koch, the Munich school of hygiene founded by Pettenkofer lost ground. Their doctrines were no longer regarded as of such prime importance. Why indeed study the conditions under which the hypothetical etiological agent of a disease might multiply in the external world when the real living organisms which caused this disease could be studied in the laboratory? In consequence of this change of sentiment attention was more and more devoted to the sick patient and the paths by which the infectious agents were eliminated from his person. Especial impetus was lent this effort by the results obtained from the further study of the cholera vibrio. The perfection of a method by means of which the spirillum of Koch could be cultivated from the dejecta within 18 to 24 hours was indeed a wonderful boon to the new sanitarians. The recognition of Asiatic cholera in its early stages and the quarantine of a country against infected individuals constituted a far simpler procedure for controlling this disease than was furnished by the elaborate measures of Pettenkofer and his pupils.

The cultivation of the typhoid bacillus by Gaffky in 1884 was hailed with almost as much enthusiasm as greeted the discovery of the cholera vibrio by Koch. The etiology of another disease was settled. The control of another pestilence was brought to medicine by the bacteriologist. Nothing is more striking in the history of bacteriology than the bitter disappointment which followed Gaffky's achievement. The typhoid bacillus proved hard to differentiate from the other microörganisms of the intestinal tract. It had no characteristic morphology which would call attention to its presence in suspected individuals. Its cultural properties were somewhat difficult to work out and only the most skillful bacteriologists could identify it with any degree of certainty. Finally the organism could not be found in such vehicles as water and milk even though fairly complete epidemiological evidence could be presented to show that the disease was spread through their agency. Despite constant efforts to solve the problem, the life history of the typhoid bacillus outside the human body remained shrouded in mystery. The hygienists of the old world were thus forced back to adopt the preventive measures against typhoid fever originally advocated by Pettenkofer, even though the infectious agent of the disease was now in their grasp. The measures suggested by the Munich school continued to be employed. Pure water was brought to the great centers of population from remote and unoccupied areas, or the water at hand was purified by filtration, the garbage of the cities was destroyed by incineration and the sewage so treated that its noxious properties were eliminated.

In consequence of these sweeping reforms in municipal hygiene, typhoid fever, which had previously been one of the most widespread diseases in Germany became one of the rarer. The experience of the city of Hamburg may be cited to indicate how effective the work of the sanitarians had become in controlling this disease. The great cholera epidemic in this city in 1892 had emphasized the rôle of impure water in the spread of Asiatic cholera and extensive filtration plants were established to purify the water of the river Elbe. Other hygienic changes were instituted at the same time in this ancient commonwealth under the direction of Professor Dunbar, a pupil of Gaffky. As a result of the measures adopted, not only did cholera die out of Hamburg, but typhoid fever as well. So effective indeed was the work of sanitarians throughout Germany that the water-borne diseases diminished steadily in frequency from year to year. In Prussia, for instance, where the typhoid mortality had at one time been so high as to have a definite influence on the total mortality, it fell from 2.4 deaths per 10,000 living, in 1889, to 1.33 in 1899 and 0.81 in 1902 (Kirchner (1)).

Typhoid fever, nevertheless, was by no means under control in Germany. It still continued to appear in the smaller towns and villages and in the country districts. Occasionally great epidemics broke out, as in Berlin in 1887-1888, where the disease was traced to an infected water supply and in Westphalia in 1900-1901, where 3000 cases and 350 deaths were attributed to the same cause. The more accurate study of the disease, moreover, indicated that other agencies than water might be operative in carrying the infection from person to person. The importance of milk especially, as a means of transmission, was brought out in Hamburg, as in Sweden, where the public dairies were found responsible for many cases of the disease.

The obscure points in the epidemiology of typhoid fever had long been recognized by Robert Koch, who was clearly aware of the difficulties connected with the isolation of the typhoid bacillus from the stools, and its early identification in the laboratory. To no one more than to the discoverer of the cholera vibrio was the necessity apparent of finding means of establishing a rapid diagnosis of typhoid fever by methods

similar to those which were employed for Asiatic cholera. At Koch's suggestion, and under his personal direction, the members of the staff of the *Institut für Infectionskrankheiten* in Berlin undertook a thorough systematic study of Gaffky's bacillus in all its phases. So many improvements in technique were soon introduced in the Berlin Institute, and also in a number of other bacteriological laboratories, that by the year 1902 Koch thought the time was ripe for inaugurating a new movement. Among the most important advances in knowledge which placed the diagnosis of the disease and the recognition of the typhoid bacillus upon a firm basis, should be mentioned the discovery of the agglutinins by von Gruber and Durham, the special media of v. Drigalski and Conradi, and the technical methods devised by Endo, Ficker and Lentz. (The importance of the fermentation tube introduced by Theobald Smith for the study of the typhoid-colon group of organisms has apparently never been recognized in Germany.) On November 28 Koch (2) proposed at the meeting of the Scientific Senate of the *Kaiser-wilhelms Akademie* that the campaign against typhoid fever should be taken up from a different standpoint. He called attention to the old Prussian law of 1835, 8, VIII, which provided that certain measures should be adopted to control the spread of a prevalent disease of the times. The disease, as we now know, was a conglomerate, including cases of spotted fever (*Flecktyphus*), recurrent fever (*Rückfallfieber*) and typhoid fever (*Unterleibtyphus* or *Abdominaltyphus*). To ward off an attack of the disease the measures provided for the avoidance of crowded rooms, pure air, cleanliness and dietetic regulations. To prevent its spread the sick should be separated from the well by isolation, their houses should be placarded, and, after recovery, the effects and the dwellings of the patients should be disinfected. The framers of the law evidently believed that the disease was communicable from person to person. Koch also called attention to the widespread doctrine deeply engrained in the minds of the medical public that typhoid fever was chiefly water-borne, despite the early recognition of its contagiousness and despite the clear evidence that the infectious material could be conveyed directly from individual to individual, as from the sick patient to the doctor, the nurse, or the orderly. Koch further emphasized the continued occurrence of the disease in the country districts, especially in the Rhine provinces and in some of the cities like Metz, Strassburg, and Saarbrücken, which had been the scenes of important battles between the Germans and the French. It seemed indeed as if a large part of the typhoid fever still found in Germany was the heritage from the war with France, remaining uncontrolled in those districts which had a French population or which had been occupied for some periods of time by French troops.

The danger to German military power arising from these constant epidemics of typhoid fever in Alsace-Lorraine was clearly recognized by the authorities. As Bismarck the Iron Chancellor had said, the Rhine provinces would always be the seat of conflict between France and Germany, the threshold of wars between the rival countries. They should, therefore, be under the power and control of Germany. Little advantage could be expected from this German control, however, unless the infectious diseases there could be regulated, especially such pestilences as typhoid fever.

Following Koch's suggestion, a trial typhoid station was established at Trier, the district which more than all others in Prussia had persistently had a high mortality from typhoid fever. The work here was undertaken by Prof. Frosch, Dr. v. Drigalski and Dr. Conradi and various prophylactic measures were tried out by these investigators to determine whether they were capable of application on a more extensive basis. When the work began at Trier, seven cases of enteric fever had been reported to the authorities. By careful examination of the population of this community and especially by a painstaking study of a large number of individuals suffering from obscure symptoms of illness, their blood being tested for agglutinins, their urine and stools being examined for the typhoid bacillus, it was soon brought to light that there were in reality not seven but sixty-four cases of typhoid of whom 70 per cent were in children. These cases were carefully isolated, their effects and dwellings disinfected. In three months the investigators believed that the four villages in the district of Trier, Waldweiler, Schildingen, Heddert, and Mandern were free from typhoid fever. No hope was entertained, of course, that this freedom would persist. A number of important advances in our knowledge of this infection were brought out by this work in Trier. Not only was it established that many mild attacks of fever without the classical typhoid symptoms were in reality genuine cases of the disease, but it was clearly shown that, contrary to general belief, children were particularly susceptible to infection. This was a point of considerable epidemiological importance, since the range of activity of children, especially of boys between the ages of eight and fifteen, is far greater than that of adults. Imagine the number of different localities the average boy will visit and the number of different individuals he will come in contact with on a long summer day, in a little village community. Possibly, however, the contribution of the greatest importance which came from this first typhoid station was the conception of the "bacillus carrier." From the observations of Frosch, v. Drigalski, and Conradi in Trier on typhoid fever, it was shown that the typhoid bacillus is present in the dejecta in two groups of individuals. One group includes those persons who have recovered from characteristic attacks of the disease and who continue to harbor and excrete the organism for long periods of time, the chronic excreters or *Dauerausscheidern*. The second group includes those individuals who have been infected with the typhoid bacillus, who have no symptoms of the disease or symptoms so mild as not to present themselves and yet give off the typhoid bacillus for indefinite periods, the chronic carriers, *eigentliche Bacillenträger*.

With the station at Trier as a model, others were established at points where typhoid was especially prevalent, as at Saarbrücken, where the second was located. July, 1903, may be said to mark the beginning of the systematic campaign against typhoid fever in southwest Germany. Eleven stations were instituted, four principal ones at Saarbrücken in Trier, at Landau in the Bavarian Rheinpfalz, at Metz in Lothringen,

and at Strassburg in Unterelsass, and seven accessory ones at Saarlouis, Neunkirchen, and Idar in Trier, at Kaiserslautern in the Rheinpfalz, at Diedenhofen in Lothringen and at Hagenau in Unterelsass. How closely these stations corresponded in location to important points of the Franco-German war is evident from the establishment of principal stations at Metz, Strassburg, and at Saarbrücken, the three communities which possibly as much as any others were the site of stubbornly fought campaigns in this great conflict.

By the end of the year 1904 these eleven institutes were established upon an orderly and lasting basis, *Herr Geheim Regierungsrat* Schneider of Hannover being selected to control and regulate the entire organization. Since then the work has gone steadily on, the men selected to direct the various laboratories showing an enthusiasm for their work, and an appreciation of its significance, both hygienic and political, which is almost without parallel. While three of the institutes originally established have been abandoned, the powers and privileges of the others have been amplified. The example of Prussia has not only had a beneficial effect upon her immediate neighbors, three stations being established by the Bavarian Government shortly after the movement was inaugurated by Prussia, but an enormous interest in the study of intestinal infections has been stimulated over the entire civilised world.

As a result of this systematic campaign against typhoid fever our knowledge of the disease has been increased during the past ten years, one might say, almost ten-fold, and one need but glance over the pages of the *Klinisches Jahrbuch* to realise the great extent of this work and the importance of the many publications which have come from these various laboratories. Indeed our entire conception of enteric fever has undergone a great change, and while we still recognize the fact that water, milk, and food may serve as the means of transmitting the infectious material from person to person, we are more and more convinced that in certain communities at least the majority of cases are due to contact either with a case of the disease or with a bacillus carrier. How easily the living organisms may be carried from sick to well is shown by such observations as those of Seige (3), who describes a house in Alsace-Lorraine, where he found a typhoid patient lying on a bed covered with a rubber mattress. The urine and the dejecta of the patient had been spilled upon this mattress, had then fallen to the floor and there been allowed to dry. In the same house Seige found a flask of disinfectant left by the medical attendant, with its cork still intact. Or the observations of Frosch (4) may be cited, who saw a woman empty the vessels containing the urine and feces of her typhoid-stricken husband in the intervals of preparing the evening meal for the other members of her family. How simply a bacillus carrier can give rise to a milk epidemic of the disease is quoted by the same author, who noticed a maid who had just recovered from a characteristic attack and who was known to harbor and excrete the organisms going directly from the water-closet to the dairy where, without even washing her hands, she began her daily task of milking. Furthermore, the extent to which the typhoid bacillus is given off by patients and convalescents has been found to be far greater than previously supposed. Frosch (l. c.) has pointed out that the bacillus is found in 80 per cent of all cases for a period of three to four weeks after the termination of the fever and Lentz (5) has shown that the excretion of the organism, if it does not cease within ten weeks, lasts almost indefinitely. In such cases this species seems to replace the normal bacteria of the intestinal tract, appearing in the dejecta in large quantity, sometimes in almost pure culture. If the organisms persist primarily in the gall bladder, from which point they find their way into the intestines, they must indeed find in the bowel itself favorable conditions for an enormous multiplication. Their presence in the dejecta of certain individuals is far too great to permit us to believe that they are harbored in the gall bladder alone. The organisms, moreover, are fully virulent, agglutinate with an anti-typhoid serum, and give the Pfeiffer phenomenon. So far as laboratory tests go, they have the same characteristics as those isolated from an acute case of enteric fever. Finally, as Prigge (6) has indicated, by far the greater proportion of the chronic carriers are women. Thus far no drugs have been found which have any lasting influence upon the number of typhoid bacilli given off by these individuals or the length of time they may continue to harbor and excrete the organisms.

While the literature describing the methods of this campaign in Germany is ample and the many important results obtained have been published with great care, a full appreciation of the inner working of a typhoid station is manifestly difficult to obtain from reading alone. The personal factor, the spirit and enthusiasm which the director of a laboratory inspires in the group of workers gathered about him, seldom if ever appear in the pages of a printed report. Feeling the inadequacy of my knowledge of the subject and desiring to acquaint myself with the more intimate details of this great work, I took occasion last September to go to Saarbrücken, where one of the principal stations already referred to is located. Through the kindness of the Director of the Institute, Dr. Prigge and his assistant, Dr. Rommeler, I was permitted to spend several days in the laboratory and was shown the practical organisation of an anti-typhoid station.

Saarbrücken is situated a little over a hundred miles from Strassburg and was the scene of many stirring events in the war of 1870. It has at the present time about 100,000 inhabitants and is the center of important mining and manufacturing industries. The people in the city itself and in the surrounding country districts are a curious mixture of races. The original inhabitants seem to be of French origin. While not speaking French, the language still prevalent in a large part of Alsace-Lorraine, the peasants, to the casual observer at least, resemble the French much more than the Germans in general physiognomy and characteristics. Added to this indigenous population is a large element of Prussians, principally workmen who have moved there in considerable numbers to take the situations offered in the mines and factories. Finally a corps of the German army is quartered in the city of Saarbrücken, adding a new and important strain to this heterogeneous population. From this country typhoid fever has never disappeared.

Epidemic after epidemic has visited the city of Saarbrücken, summer and winter alike, and the disease has remained endemic in small foci in the rural districts. So high indeed has been the death rate here that the first principal station to be established by the Prussian Government was located at this point.

The laboratory building in Saarbrücken, where the work of the station has been carried on now for eight years, was originally a small boy's school. It contains but one large workroom fitted up with the apparatus usual in a bacteriological laboratory, a preparation room for the manufacture of media and a small office for the administrative end of the work. Provision is made for a certain amount of experimental investigation on animals in the adjoining courtyard. What a lesson for those of us who are disposed to estimate the magnitude of scientific work by the size of the buildings in which the work is done. To this station is reported every case of typhoid fever or every case of illness with typhoidal symptoms occurring in Saarbrücken and in the adjoining country for a distance of about ten miles. The population represented in these two areas is nearly 200,000. Specimens of blood from all suspected cases are sent to the station where they are tested for typhoid agglutinins and also for para-typhoid and dysentery agglutinins. In addition, the stools and urine from such cases are also sent if the diagnosis remains in doubt. For all cultures the v. Drigalski-Conradi medium is employed in large Petri plates measuring 7-8 inches in diameter. All blue colonies which develop on these plates are immediately tested with a powerful anti-typhoid serum, an anti-para-typhoid and an anti-dysentery serum. Should agglutination of the organisms occur with any of these sera, the organisms are cultivated and identified. As soon as a diagnosis of typhoid fever is established in any case the patient is removed to the hospital in Saarbrücken. This removal is practically compulsory. The sanitary regulations provide that all cases must be sent there unless adequate arrangements can be made elsewhere for their isolation and proper care. Since the population of the district, especially outside the city limits, is extremely poor, it is very exceptional for a typhoid patient to be kept at home. While in the hospital the cases are entirely under the control of the hospital authorities, the blood, urine, and stools being examined in the laboratory there and not at the station. A convalescent can only be discharged after two consecutive examinations have failed to reveal the typhoid bacillus in his dejecta. If, however, the organisms persist beyond a period of ten weeks, then the individual can no longer be legally or forcibly prevented from leaving the institution. He may go when and where he chooses. In such cases the sanitary acts provide only that the infected person must be informed of the danger he exerts towards the people with whom he comes in contact and that he must be instructed in the methods to be employed for the disinfection of his excreta. To determine the length of time these remain infectious he must send samples or urine and stool to the laboratory for examination or permit members of the laboratory force to collect such samples from his premises. This provision gives the station its control of the population of the district. Every bacillus carrier is known and watched. Large charts in the institute show the location of every house where typhoid fever has occurred during the past eight years and the dwelling of every known carrier. Whenever a new case of the disease occurs, or a small epidemic breaks out, the association of the new cases with the old can be worked out, sometimes with apparent ease.

Following the removal of any typhoid patient to the hospital, the district physician (*Kreisarzt*), in company with some member of the staff of the institute, visits the premises of the infected person. A careful survey of all the sanitary arrangements of the place is undertaken, especially those concerned with the disposal of excreta and garbage. The water, milk, and food supplies are thoroughly looked into. The members of the family are questioned as to the possible source of infection. Finally all the other inmates of the dwelling are overhauled, to determine the existence of any mild or concealed cases of enteric. On the appearance of the slightest symptoms suggestive of a typhoid infection, specimens of blood, and frequently of urine and stools are sent to the laboratory for study. In this way nearly all the cases of typhoid fever which may occur among the patient's associates in the district of Saarbrücken are eventually brought to light.

I had the pleasure of accompanying Dr. Engels, the district physician and Dr. Rommeler of the institute, on several trips, and I could not but be impressed by the thoroughness with which the inspection was made and the wisdom of the measures suggested, always touching the essentials of cleanliness and yet always, as far as possible, within the means of the families visited. Most interesting was the harmony which apparently existed between the populace and the representatives of the authorities. On the one side the poor people showed themselves thoroughly amenable to instruction and advice from the physicians, and on the other side the physicians were careful not to wound their tender susceptibilities by impertinent questions, yet were determined to get to the bottom of the case and anxious to make effective recommendations. It was evident that courtesy and tact were just as necessary to success in this work as scientific knowledge. In all instances, before the inspection was completed, the families of the patients were carefully advised in regard to the cleaning and disinfection of the infected bed-clothing and wearing apparel and warned of the necessity of immediately isolating any other members of the family who should develop symptoms of illness. Finally, a complete history of the case is written up, embracing the work of the station, of the hospital authorities, and of the district physician, the case is charted at the station and a copy of the history forwarded to the officials at Berlin.

By this very elaborate system the extent and the distribution of typhoid fever in Saarbrücken is worked out to the finest detail, the most accurate knowledge of the bacillus carriers is obtained and the various hygienic measures necessary to stamp out the disease are learned. The sanitary authorities are kept informed of any unhygienic conditions which may be found in the community and measures looking towards the improvement of the water supply, the sewage and garbage disposal are constantly being put in force.

Many interesting details of this great work are related by the bacteriologists connected with the Saarbrücken institute. Some of these indicate the great difficulties of the investigation, while others show the skill with which the authorities have run down their quarry. They illustrate also how tenderly and carefully the population must be handled if results are to be obtained. Early in the campaign, for instance, attention was called to the continued occurrence of typhoid fever in one particular farm-house. The disease was constantly breaking out among the new servants coming to the place while the family of the farmer never seemed to be long free from attacks. During a period of six or seven years as many deaths occurred among the servants or in the farmer's children. A carrier was naturally surmised and suspicion was finally directed to the aged grandmother as being the person in question. All efforts to obtain samples of her urine or stools were fruitless. She stubbornly refused to send any material for examination or what was sent was not believed to be her own. Finally an epidemic of the disease broke out in the vicinity and on some pretext or other the old woman was persuaded to enter the hospital for a few days. Here it was at once established that she was a chronic excreter, her attack of typhoid apparently dating back nearly thirty years.

On another occasion a poor unfortunate bacillus carrier was heard bemoaning her fate to one of her neighbors. Every time her excreta were sent to the station she was informed that she was still "sick" and sick she must remain, an object of suspicion to family and friends. "What a fool you are," said her neighbor. "Just send the dejecta from your daughter and in two weeks you will be perfectly well." And that, of course, is the unfortunate truth.

In thus watching the anti-typhoid work at Saarbrücken and talking intimately with the bacteriologists there my greatest interest naturally lay in getting an expression of opinion from them as to the efficacy of the measures employed and as to the eventual outcome of the movement. They were agreed that the actual amount of typhoid fever in Saarbrücken was constantly decreasing, even though it was difficult to bring statistical evidence to prove this point. The great increase in the number of cases of the disease brought to light by the careful study of the population offset the diminution in number which resulted from their rigorous preventive measures. Their yearly statistics were frequently ruined, moreover, by the appearance of the disease in epidemic form. The actual number of epidemics is becoming constantly smaller, however, and the epidemics, which do arise, are more quickly brought to a standstill. The disseminated typhoid is becoming less common, and more important than anything else the number of bacillus carriers is steadily diminishing. Certain areas in the district also, which formerly were infected with typhoid fever, are gradually becoming free from the disease. In general, the typhoid has disappeared more completely from those areas where the hygienic conditions have been improved, especially where a properly controlled supply of pure water has been obtained, than in those regions where the conditions are still bad.

In Saarbrücken, as in every country where typhoid fever is prevalent, the chronic carriers are the great obstacle to the complete elimination of the disease. They are perfectly well individuals and in the eyes of the government entitled to just as full a measure of freedom and protection as are other individuals. Yet they are a constant menace to family and friends, are viewed with suspicion by the local authorities and are apt to become pariahs in the communities where they dwell. Their fate is a hard one and wise indeed will be the government which will learn to provide for their comfort and happiness and yet rob them of the danger they exert towards the individuals with whom they come in contact. Thus far no measures looking to their segregation have ever been adopted by the German authorities and it is hardly likely that such measures could be passed. It has been suggested that legislation might be enacted forbidding bacillus carriers engaging in any occupation where the handling of food comes into play. Despite the pressure which is constantly being exerted to bring about such legislation, the government has steadily refused to enact it. The problem of the bacillus carrier is not, however, a problem for Alsace-Lorraine alone, but for all countries where typhoid fever exists. Whether the solution of this problem lies in preventive legislation or in the field of specific therapy, the problem must eventually be solved if the disease is to be controlled.

After a visit to a typhoid station and even a brief study of the methods employed and the results obtained, one cannot but marvel at the genius of Robert Koch, who with far-sighted wisdom suggested this new plan of campaign against one of the most devastating of our modern pestilences, at the value of that form of paternal government which listens to the advice of its scientific men and seeks to put in practical operation the plans they may outline, and at the energy and industry of its citizens who devote their lives to carrying out its edicts.

BIBLIOGRAPHY.

1. Kirchner: Klin. Jahrb., 1907, XVII, 433.

2. Koch: Die Bekämpfung des Typhus. Berlin. A. Hirschwald. 1903.

3. Seige: Klin. Jahrb., 1905, XIV, 507.

4. Frosch: Klin. Jahrb., 1907, XVII, 115.

5. Lentz: Klin. Jahrb., 1905, XIV, 475.

6. Prigge: Klin. Jahrb., 1910, XX, 245.

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ON THE SEASONAL VARIATIONS IN THE BACTERIAL FLORA OF THE BALTIMORE CITY WATER.

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During the past two years the Baltimore city water has been subjected to routine examination in the bacteriological laboratory of The Johns Hopkins University. The source of the water supplied to the laboratory is the Gunpowder River by way of the reservoirs of Clifton Park and Lake Montebello. For the same period many samples of water have been collected from the Gunpowder River itself and from its various branches. This source of supply represents only a part of the total quantity of water distributed in Baltimore, the rest being derived from Jones Falls and Lake Roland. In a previous communication,[1] we have called attention to the serious and permanent pollution of the Gunpowder River, its danger to the city and the possibility that the typhoid fever in this community may be associated with the immense amount of fecal material which is constantly being poured into our surface supply. The huge rural population dwelling at various points along the Gunpowder watershed explains clearly the source of this fecal pollution of the river and the occasional appearance of typhoid fever in this population, as pointed out by Price, Stokes, and Rohrer,[2] suggests that at almost any time this fecal pollution may become a typhoid bacillus pollution.

Our observations on the character of the Gunpowder water are indentical with those of Stokes and his co-workers at the City Department of Health, and Stokes and Hachtel[3] have reported a serious contamination of Lake Roland and the small creeks which empty into it. In our previous studies on this subject, it was established that the period during which the typhoid fever in Baltimore was at its height in the season of 1910 was also the period when the pollution of the water supply was greatest. This coincidence, while not a proof that our typhoid is water-borne in character, is very suggestive. At the same time the scattered distribution of the cases of this infection in our city is in harmony with the theory that the disease is to be attributed, at least in large part, to its badly polluted drinking water.

In this investigation of the Gunpowder River the regular methods of counting the colonies on agar and gelatin plates and of determining the presence of *Bacillus coli* by planting Smith fermentation tubes with varying quantities of water have been employed. The results of our work along this line have already been published, and one of us has called attention on a previous occasion to some of the organisms which may be found in the Gunpowder and its tributaries.[4] Recently, during a period of eight months the water varied in character from *badly polluted*, at a time of very hot dry weather, showing a positive presumptive test for *Bacillus coli* in 1/1000 of a cubic centimeter, to *fairly pure*, giving this test only in quantities of 5 to 10 cubic centimeters, the number of organisms on the plates showing corresponding fluctuations. We have therefore attempted to gain further information in regard to bacterial pollution of water by a consideration of the variations in frequency exhibited by the several species from time to time. For this purpose we have poured agar plates regularly from the fermentation tubes in which the presumptive test for *Bacillus coli* was positive, picked out on these agar plates all those colonies which might be regarded as more or less characteristic of the intestinal bacteria, transferred them to agar and made a study of their cultural reactions. The colonies selected corresponded in general to such as are produced by *Bacillus coli*, being slightly raised, grayish white, moist, glistening, with well defined edges. In addition to these, we have also transferred the spreading colonies of *Bacillus proteus vulgaris* and the porcelain-white sticky growths typical of the encapsulated bacteria. We have thus studied practically all varieties of bacteria appearing on our plates except the pigmented and spore-bearing species. After the organisms were seeded on agar a careful investigation was made of the morphology, motility, and tinctorial properties of the various isolations and of their cultural reactions in agar, gelatin, broth, milk, potato, and with dextrose, saccharose and lactose in Smith fermentation tubes. The manner in which dextrose is decomposed was especially observed and the ratio of hydrogen to carbon dioxide was determined with all the fermenting bacteria. These cultural reactions were read at 37° C. except in the case of gelatin, readings being made at the end of 48 hours and 10 days. As far as possible the cultural characters of each isolation were carefully studied, but the attempt was made not so much to work out any particular strain with great detail as to classify the organisms on broad general principles in certain well-defined groups. The following species have been isolated and studied, and their relative frequency at various times estimated.

Bacillus coli Escherich.

This species was present at all times in the Gunpowder water. Only organisms with a characteristic morphology and motility, negative to Gram's stain, producing moist glistening growths on agar, failing to liquefy gelatin, acidifying and coagulating milk, fermenting dextrose and lactose with gas and acid production, the gas in dextrose consisting of hydrogen and carbon dioxide with the formula $\frac{H}{CO_2} = \frac{2 \text{ to } 3}{1}$ were included. An abundant yellow-brown growth on potato was shown by the majority of the isolations and in general a positive indol test was given.

During the period of greatest pollution *Bacillus coli* could be isolated on nearly every occasion from those fermentation tubes which were planted with 1/100 of a cubic centimeter, and on one

occasion it was obtained in a dilution of 1 to 1000. At that time the agar counts showed from 500 to 2500 bacteria to a cubic centimeter. Of the non-pigmented non-sporebearing colonies which appeared upon the plates, however, only about 25% proved to belong to this type. Subsequently, when the water was comparatively pure, the presumptive test being obtained from 5 and 10 cubic centimeters, with a bacterial count running well under 1000, it was found that this organism comprised over 50% (55%) of the characteristic colonies.

Bacillus cloacae Jordan.

Organisms belonging to this species were encountered constantly in the Gunpowder water. In morphology and motility they resembled *Bacillus coli* except that in general the individual elements were a little larger. Like it they were negative to Gram's stain. On agar they produced a bluish-gray opalescent growth. In gelatin a napiform liquefaction occurred in from one to nine days. Litmus milk was first acidified, then coagulated, and later the precipitated casein was dissolved producing a clear yellowish serum. The carbohydrates, particularly dextrose and lactose were always fermented, and in dextrose the gases evolved showed the inverted formula $\frac{H}{CO_2} = \frac{1}{2 \text{ to } 3}$. On potato the organisms made a rather dirty yellowish or yellowish-brown growth. The reactions for indol were negative.

Representatives of this form occurred at all times, both at the period of greatest fecal contamination when the presumptive test was positive in 1/10 and 1/100 of a cubic centimeter, and in the time of relative purity when 5 and 10 cubic centimeters of water were required to give this test. When the pollution was at its maximum this species comprised about 10% of the intestinal colonies found, while in the period of purity about 25% of the colonies fished proved to belong to this group. It fluctuated in number therefore in much the same way as did *Bacillus coli*.

Bacillus fæcalis alkaligenes Petruschky.

A regular inhabitant of the Gunpowder water is an organism which we regard as *Bacillus fæcalis alkaligenes* of Petruschky. On many of the plates poured from the fermentation tubes were found colonies indistinguishable from those of *Bacillus coli* in size and shape, but usually somewhat flatter and more translucent. When transferred to agar they grew upon this medium in a manner resembling that of *Bacillus coli*. Morphologically they were somewhat longer than this organism however and were actively motile, often growing in chains or threads. They were negative to Gram's stain. They failed to liquefy gelatin, fermented none of the carbohydrates, growing only in the open bulb of the fermentation tube where the reaction was alkaline, and produced an intense alkaline reaction in litmus milk without coagulation. On potato the organisms developed in a grayish-white moist layer. The test for indol was usually negative. The bacteria which we consider *Bacillus alkaligenes* are identical in reactions with the bacteria of the same species which we have frequently found in the contents of the intestinal tract.*

This species, like the two preceding, occurred constantly in the city water. During the period of greatest pollution it comprised only about 10% of the intestinal colonies however, but at the time of relative purity about 15% of these colonies proved to be *Bacillus alkaligenes*.

Bacillus proteus vulgaris Hauser.

On many occasions spreading colonies were found on the agar plates and when transfers were made the organisms cultivated proved to be representatives of the proteus vulgaris group. Morphologically these organisms were long slender rods with a marked tendency to form threads and chains. They were usually actively motile, but showed the periods of quiescence alternating with periods of activity characteristic of proteus. They decolorised by Gram's method. On agar the organisms produced a slimy, moist, glistening, spreading, rather watery layer. Gelatin was rapidly fluidified with a saccate liquefaction. In milk acid was first shown and usually a soft coagulum. The reaction soon became intensely alkaline and the casein was converted into a clear dark yellowish serum. Dextrose was fermented with the formation of acid and the evolution of a gas with the formula $\frac{H}{CO_2} = \frac{2 \text{ to } 3}{1}$. On potato the growth was raised and had a dirty yellowish color. In all albuminous media the organisms evolved a disagreeable odor of putrefaction.

This species was found nearly every week in the city water, comprising about 10% of the intestinal forms during the height of pollution, but appearing also in the time of relative purity when about 5% of the colonies transferred belonged to it.

Liquefying Fermenting Organisms.

One of us (*l. c.*) has previously called attention to a peculiar type in the Gunpowder water which bore a close resemblance to *Bacillus coli*, but was easily to be distinguished from it by its liquefaction of gelatin. The individual bacteria in this species were short and plump in form and showed a moderate motility like that of *Bacillus coli* and like the latter species were negative to Gram's stain. The agar colonies were round and circumscribed and on slant agar the organisms produced a moist glistening grayish-white growth indistinguishable from that shown by the bacillus of Escherich. Milk was acidified and coagulated and the casein slowly peptonised. On potato the growth was profuse, a dirty grayish-white layer which later became yellowish-brown. No indol was present. Both dextrose and lactose were fermented, and in dextrose the gas evolved had the regular formula $\frac{H}{CO_2} = \frac{2 \text{ to } 3}{1}$.

These reactions, with the exception of milk, are thus seen to resemble those of *Bacillus coli*, and a provisional diagnosis of this species was frequently made. In the gelatin tubes the organisms first grew as a delicate white line along the line of inoculation and spread out slightly on the surface of the gelatin at the point where it had been punctured by the needle. After the lapse of two or three days, however, liquefaction of the gelatin occurred and proceeded slowly along the line of inoculation in a saccate form leaving a firm hard base of solid gelatin covered over by the fluidified medium. Frequently a line of bubbles like a string of beads or pearls was seen, extending from the central part of the tube in an upward direction, and

* Some difficulty is always met with in identifying *Bacillus alkaligenes* when isolated from water owing to the resemblance which it bears to certain well-known fluorescent bacteria, especially *Bacillus fluorescens non-liquefaciens*, the cultural reactions of which are almost the same. If the former species happens to be very slow in developing its fluorescent pigment, it may be mistaken for *Bacillus alkaligenes*. The strains which we have identified as the bacillus of Petruschky were kept in the laboratory for from eight to ten months and at no time could a fluorescent pigment be detected.

this appearance was often the first indication that liquefaction was beginning. This was found so constantly that we came to regard it as rather characteristic.

These organisms evidently form a distinct and well-defined species. The representatives which we have recently isolated are indentical with some found previously in the various tributaries of the Gunpowder River, in samples of spring water sent to the laboratory for examination, and in specimens of the Baltimore sewage. Occasional obscure references in the literature may be found to bacteria with these reactions and the term "liquefying coli" has been applied to them.[5] The species is easily differentiated from *Bacillus coli* by its liquefaction of gelatin, and it more closely resembles *Bacillus cloacae* than any other organism. We have separated it from *Bacillus cloacae* because of the gas formula, one of the principle cultural reactions of Jordan's bacillus being the production of a gas composed chiefly of carbon dioxide. According to Fuller and Johnson,[6] and Winslow,[7] however, it might be included in the cloacae group.

This liquefying fermenter had a peculiar place in our city water. During the time of greatest pollution it was frequently isolated, fully 10% of the intestinal colonies belonging to this species. It was found in the fermentation tubes which gave a positive test from the smallest quantities of water, from 1/100 and from 1/1000 of a cubic centimeter. Subsequently when the amount of pollution diminished the water becoming relatively pure, these organisms seemed to disappear entirely from our plates.

Bacillus lactis ærogenes Escherich.

A number of strains giving the reactions of the lactis ærogenes group were encountered in various plates poured from the fermentation tubes. Morphologically they were thick, plump, nonmotile bacteria, negative to Gram's stain. On agar plates they made heavy, raised, porcelain-white colonies, and on agar slants a raised convex growth along the line of inoculation. Both colonies and slants on agar showed a mucoid consistency with a tendency to string out in fine threads when touched with the platinum wire. In gelatin the organisms developed well along the line of puncture and spread out on the surface as a convex raised porcelain-white knob. The growth on potato was heavy, moist, yellowish-white in color with a strong cheesy odor. Dextrose, saccharose and lactose were all fermented with the production of acid and gas, the gas formula being $\frac{H}{CO_2} = \frac{1}{1-2}$. In litmus milk an abundant acid developed followed by a rapid coagulation. In this medium capsules could be demonstrated in some cases. While we regard the presence of capsules as an essential characteristic for the lactis ærogenes group we have in the present study included not only organisms with the cultural reactions mentioned above in which capsules were actually stained, but a number of isolations with the same reactions in which capsules were not proven. The morphology and lack of motility of the organism and their mucoid colonies of a sticky consistency indicated that they belonged in this group. (See Fuller and Johnson (*l. c.*) and Winslow (*l. c.*).)

The *Bacillus lactis ærogenes* was obtained from the Baltimore city water only during the period of greatest pollution when the presumptive test for *Bacillus coli* was positive in a dilution of 1-100. At this time about 10% of the colonies picked proved to be this organism. Later, when the pollution of the water had diminished in intensity mucoid colonies were no longer found on the plates poured from the fermentation tubes.

Intermediate Group.

On a few occasions we encountered bacilli which could only be placed in the intermediate, Gärtner, or Hog Cholera group. These organisms resembled *Bacillus coli* in morphology and motility, were negative to Gram's stain and produced on agar a moist, rather thin, translucent growth, indistinguishable from that formed by this species. In gelatin the growth was abundant along the line of puncture and on the surface, no liquefaction resulting. In milk a preliminary acidity was observed followed by an alkaline reaction. Dextrose was fermented with a gas formula $\frac{H}{CO_2} = \frac{2 \text{ to } 3}{1}$ but neither saccharose or lactose was acted upon. A yellowish-brown growth was seen on potato, and the test for indol was negative.

Organisms belonging to the intermediate group were found but rarely in the city water except in the height of pollution at which time they formed about 5% of the intestinal colonies.

Attenuated Forms.

In addition to these organisms with well-defined characters a great many others were isolated from time to time and their cultural properties tested. Many of these turned out to be attenuated forms of easily recognised species. When originally obtained their reactions were inconstant and difficult to interpret. This was especially true in regard to the carbohydrates, which showed merely an acidity with sometimes a bubble or two of gas. By transferring these organisms daily from fermentation tube to fermentation tube their activities were increased so that eventually they caused an abundant evolution of gas. Such cultures could easily be classified after their reactions on the culture media had become fixed, and they were then found to belong to the types of *Bacillus coli*, *Bacillus cloacae*, *Bacillus proteus vulgaris*, or to the "liquefying fermenters." The rejuvenated *Bacillus coli* proved to have very constant reactions, the transfers to solid media retaining their properties and continuing to split the carbohydrates vigorously. The proteus and cloacae cultures, however, when grown for some time upon solid media, reverted to their inconstant character, producing but little change in the carbohydrates. At the same time descendents of these strains which were transferred from Smith tube to Smith tube, retained their ability to ferment the sugars actively.

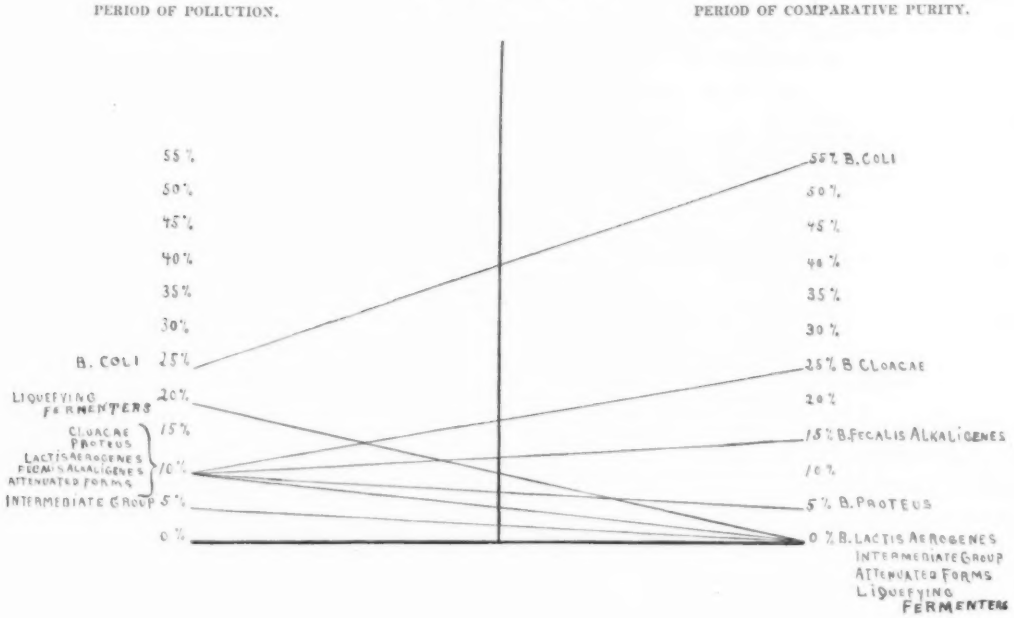
We have placed these attenuated forms together because of their occurrence in larger numbers at the period of great pollution. At the time when fermentation was produced by small quantities of the city water, 1/100 of a cubic centimeter, about 10% of the colonies picked gave these attenuated forms. Later, when the serious pollution disappeared, the organisms isolated were much more fixed and definite in character and presented little or no difficulty in identification, few attenuated forms being encountered.

Discussion.

By reference to the accompanying chart, which represents the relative frequency of the various organisms described above, it may be seen that as the Baltimore city water changed from a condition of extreme pollution to one of relative purity there was a qualitative change in the bacterial flora as well as the quantitative one which has previously been indicated (*l. c.*). It might be expected *a priori*, and on the basis of analogy with the changes which Winslow (*l.c.*) has shown to occur in sewage on storage, that when the filth in the Gunpowder water was concentrated, as in the severe drouth which marked the season

Relative Proportion of Organisms.

Baltimore City Water.



when these examinations were begun, the period of high pollution, the bacteria representative of fecal contamination would merely appear in greater numbers. As a matter of fact, the change in the bacterial flora was far more fundamental than this. Organisms were found at the time of pollution which were not usually present in the Gunpowder water, while the bacteria ordinarily found there and indicative of fecal contamination were by no means as frequent as when the supply was good. Thus *Bacillus coli*, always in evidence on the plates, during the height of contamination comprised but 25% of the intestinal forms encountered, while subsequently, when the pollution had passed away, it represented over one-half of the species present, or 55%. The same variation held true for *Bacillus alkaligenes* and *Bacillus cloacae* which rose respectively from 10 to 15% and from 10 to 25%. The relatively smaller proportion of these organisms in this period of pollution is to be explained by the appearance of forms which do not occur at all or so rarely among the bacteria found normally as not to be conspicuous, and by the increase in the members of the proteus group. About 15% of the isolations were found to belong to this latter group while later they fell to 5%. In addition *Bacillus lactis aerogenes* comprised 10% of the colonies, "the liquefying fermenters," 10%, and the intermediate group, 5%. The rest of the forms isolated, about 10%, we have placed in the category of attenuated organisms. With the extreme degree of filth we have then primarily a greater diversity in the intestinal bacteria isolated from the city water. Even if we should disregard the amount of gas and its ratio in classifying the "liquefying fermenters," which would permit them to be placed with *Bacillus cloacae* we would still have the appearance of *Bacillus lactis aerogenes*, the intermediate and the attenuated forms to account for. The frequency of these aberrant types suggests another phase of bacterial growth. Possibly when the fecal material in the water is concentrated the conditions become favorable for the survival and multiplication of certain bacteria brought into the river with the excessive amount of waste material from human or animal sources while under ordinary circumstances, when this material is diluted, such organisms may fail to survive in the struggle for existence with the bacteria ordinarily found in the water. The presence moreover of so many attenuated forms which after prolonged cultivation in the laboratory assume fixed characters, the originals from which they were derived remaining inconstant, indicates that very profound alterations had occurred in the conditions governing the life of the various organisms. The fact that this period of high pollution was also the season when our typhoid fever was at its height raises important theoretical questions as to the epidemiology of this disease. Is it possible that the hot weather of summer can offer better conditions for

the survival and multiplication of the typhoid bacillus in water, as apparently it does offer better conditions for the development of a more diversified fecal flora, than the moderate weather of the spring or fall or the cold weather of winter? With the evidence at hand this can only be suggested as an interesting line of speculation. Finally in view of the fact that the Gunpowder water at the time of extreme pollution reveals the presence in quite large numbers of the bacteria which we have designated as "liquefying fermenters," the question may also be raised whether the occurrence of these organisms in water may not be indicative of its very serious contamination. Further investigation only can settle this point.

BIBLIOGRAPHY.

1. Ford and Watson: Johns Hopkins Hosp. Bull., 1911, XXII, 351.
2. Price, Stokes and Rohrer: J. Am. M. Ass., 1912, LVIII, 163.
3. Stokes and Hachtel: Arch. Int. Med., 1910, VI, 121.
4. Ford: Johns Hopkins Hosp. Bull., 1911, XXII, 53.
5. Durham: J. Exp. Med., 1903, V, 353.
6. Fuller and Johnson: J. Exp. Med., 1899, V, 609.
7. Winslow: J. Infect. Dis., 1909, I, 170.

THE MIDWIVES OF ANNE ARUNDEL COUNTY, MARYLAND.*

By HELMINA JEIDELL, M. D., and WILLA M. FRICKE, M. D.

In an effort to solve the midwife problem in the United States there have been careful reports published of the midwifery conditions in three large American cities: Baltimore, Chicago and New York. Up to the summer of 1911, however, no investigation of conditions in the rural districts had been attempted. In these the character of the population, the industries and transportation facilities present an entirely new phase of the question. Therefore, an investigation in Anne Arundel County, Maryland, was undertaken under the direction of Dr. Mary Sherwood.†

This county was selected as a fairly typical example of the conditions existing throughout the country districts of the State, with its mixed population, native whites, foreign whites, and colored, and the varied nature of its industries, ranging from farming to oystering and canning. The means of transportation here is almost entirely by horse.

Anne Arundel County lies on Chesapeake Bay just south of Baltimore County and includes the city of Annapolis. It covers an area of 430.4 square miles. A recent census gives a population of 43,740, of which 26,775 are white, 16,965 are colored. The county is divided into eight election districts, in each of which there are usually two Board of Health subregistrars who report to the local registrar at Annapolis. All but two of the registrars are physicians. Outside of the city of Annapolis there are twenty physicians, or approximately one physician to every twenty-one square miles.

Before presenting the details of the investigation which we have conducted in this county, it may be well to give a brief summary of the requirements in this State for the licensing of midwives:

1. If in actual practise prior to July 1, 1910, a license will be issued without examination after registration with the local registrar.

2. After July 1, 1910, requirement for registration and license is the passing of an examination with the State Board of Health; applicants for examination must be qualified to read and write, must be able to fill out correctly the required birth certificate and present a certificate from a maternity hospital or legally qualified practitioner of applicant's attendance on at least five cases of childbirth, and that such applicant is competent to attend ordinary cases of labor.

The statute declares it unlawful for any midwife to make a vaginal examination, to attempt to deliver a retained placenta, to use forceps, to attempt version or any forcible delivery, and requires that in all cases of labor not normal a licensed practitioner be notified.

Report of all cases of ophthalmia neonatorum is obligatory.

We are under great obligations to Drs. Price and Beitler of the State Board of Health for their hearty co-operation and assistance. From them we obtained a list of the registered midwives. Owing to the difficulties of traveling in the county, we found it convenient to fix our headquarters in Annapolis and make trips of several days duration into the various districts where the registrars cordially gave us invaluable assistance in locating the midwives in their vicinity. Many of the houses were difficult to reach as they were miles away from the main road. In conducting the interviews with the midwives we used the questionaire prepared by the Committee on Midwifery which is similar to that employed in all previous investigations, and a tabulation of the facts obtained was prepared which appears in Tables I and II.

Of the 119 midwives practising in the county 17 or 14.28% are Americans, 95 or 79.83% are colored and 7 or 5.71% are foreigners, including 2 Germans, 2 Poles, 1 Lithuanian, 1 Bohemian and 1 Dane. Twenty are practising in the city of Annapolis.

The white midwives take only white cases. The colored midwives take white and colored cases, and the latter they deliver themselves, whereas to most of the white cases they serve only as obstetrical nurses with a physician. Three of the 119 midwives had about 75 cases a year; 1 had 65; 2 had 50; 2 had 35. The remainder averaged from 3 to 30 cases a year.

Two-fifths of the births in Anne Arundel County recorded at the Health Department are attended by midwives. In the year 1911 40% of this two-fifths were reported by three midwives. Only 33 of the 119 midwives state that they ever report births, and most of these do so only occasionally.

* This study was made possible by the generosity of the Maryland Society for the Prevention of Blindness.

† Chairman of the Committee on Midwifery of the Association for the Study and Prevention of Infant Mortality.

Of the 119 only 4 had been trained in a school for midwives. The remainder were self-taught or had worked with a physician at the bedside. One of the 4 had attended a school for midwives in Chicago for six months. Two had a six months' hospital training, one in Germany, one in Russia. One had two and a half years in a hospital in Denmark. Two colored midwives had "responded to the call of a good spirit."

Thirty-four had registered with the Board of Health; 21 of these had received licenses to practise. Only 3 had signs displayed according to the law. Seventy-seven could neither read nor write.

Practically all the midwives made vaginal examinations. nail-scissors with especial pride; 4 carried thermometers. The midwives did not count the pulse; 1 colored midwife stated that she always felt the pulse, but gave as an estimate of the normal pulse, "about two."

The fees received average from $3 to $5, although several of the white women earn as much as $10 to $25. The distances to be traveled often make it necessary for the midwife to remain at the home of the patient. In these cases, besides the confinement and nursing, her duties always include entire charge of the household. Many, however, make daily visits for ten days toiling backward and forward several miles over the country roads.

TABLE I.—119 MIDWIVES OF ANNE ARUNDEL COUNTY—PERSONAL STATISTICS.

Nationality.	Number.	Age in Years.								Residence in America.				Education.				Diploma.			License.		Registered at Health Board.		Home Conditions.			
		20 or less.	20–29.	30–39.	40–49.	50–59.	60–69.	70–79.	80–89.	1 yr. or less.	1–10 yrs.	10–20 yrs.	20 or more.	Read and Write. Yes.	Read and Write. No.	Speak English. Yes.	Speak English. No.	American.	Foreign.	None.	Yes.	No.	Yes.	No.	Good.	Fair.	Bad.	Not seen.
Americans	17	..	..	3	4	8	1	1	..	..	..	..	..	14	3	17	..	1	..	16	1	16	3	14	12	3	1	1
Negroes	95	..	..	6	19	42	16	10	2	..	..	..	..	12	73	95	..	..	..	95	18	77	29	66	20	62	9	4
Germans	2	..	..	..	..	1	1	..	..	..	1	1	..	2	..	2	..	..	1	1	..	2	..	2	1	..	..	..
Bohemians	1	..	..	1	..	..	..	..	..	..	..	..	1	1	..	1	..	1	..	..	1	..	1	..	1	..	..	..
Dane	1	..	..	..	..	..	1	..	..	..	..	..	1	1	..	1	..	..	1	..	1	..	1	..	1	..	..	..
Lithuanian	1	..	..	..	..	1	..	..	..	..	..	..	1	1	..	1	..	..	..	1	..	1	..	1	1	..	..	..
Poles	2	..	..	..	..	1	1	..	..	..	..	2	..	1	1	..	2	..	..	2	..	2	..	2	1	1	..	..
TOTAL	119	..	..	10	23	53	20	11	2	..	1	3	3	32	77	117	2	2	2	115	21	98	34	85	37	66	10	5

TABLE II.—119 MIDWIVES OF ANNE ARUNDEL COUNTY—FACTS ABOUT THEIR PRACTISE.

Nationality.	Number.	Length of Practising Years.				Methods of Practice.																Care of Infant's Cord.				Attention to Mother.		Suspected of Criminal Practise.	Receives and Cares for Patients in Home.
						Attends Normal Cases Only.		Uses Antiseptics.			Equipment and Cleanliness of Bag.			Care of Infant's Eyes Bathed Daily.			Prophylactic (Boric)			Twine and Powder or Nutmeg.	Twine and Absorbent Cotton.	Twine and Lard or Vaseline.	Sterile Tape and Aseptic Powder				
		1 or less.	2–9.	10–19.	20 or more.	Yes.	No.	Yes.	No.	Sometimes.	Fair.	Bad.	Not seen.	None.	Boric.	Water.	Breast Milk.	No.	Yes.	No.					Yes.	No.		
Americans	17	1	4	18	4	14	3	8	7	2	..	4	..	13	9	6	1	1	7	10	9	1	2	5	17	..	1	..
Negroes	95	1	19	36	39	59	36	10	71	14	..	24	..	71	21	55	3	16	8	87	28	7	57	3	89	6	1	1
Germans	2	..	..	1	1	1	1	1	1	..	1	..	..	1	1	1	..	..	1	1	..	..	1	1	1	..	..	..
Bohemians	1	..	..	1	..	1	1	1	..	..	..	1	..	..	1	..	..	..	1	..	..	..	..	1	1	..	..	..
Dane	1	..	..	..	1	..	1	1	..	..	..	1	..	..	1	..	..	..	1	..	..	..	..	1	1	..	..	..
Lithuanian	1	..	..	1	..	..	1	1	..	..	..	1	..	..	..	1	..	..	..	1	..	..	1	..	..	1	..	..
Poles	2	..	..	..	2	..	2	..	2	..	..	..	..	2	..	2	..	..	..	2	..	..	..	..	..	2	..	..
TOTAL	119	2	23	47	47	74	45	22	81	16	1	31	..	87	33	65	4	17	18	101	37	8	63	11	110	9	2	1

All professed to wash their hands with soap and water although, according to the physicians, many go unwashed directly from field labor to an obstetrical case. A number lubricated their hands and the vulva with lard or vaseline. Only 2 of the 22 who claimed to use antiseptics had any comprehension of their significance. Prophylactic silver nitrate was used by no one. Seventy-four attended normal cases only. Forty-five called in no medical assistance even for such complications as hemorrhage, retained placenta and abnormal presentations requiring version. Perineal tears were apparently not recognized at all, but three admitted their occurrence. One alone of the 119 midwives carried a bag with the requisite supplies and that was not clean. Some sort of a bag was carried by 31—the usual equipment being vaseline, a ball of twine and scissors. One displayed a pair of gilt

A history of puerperal infection, criminal abortion and ophthalmia neonatorum is quite impossible to obtain. According to one of the physicians Neisser infection was very uncommon until, within recent years, the electric lines and State roads have made communication with the city easier. Only two midwives were suspected of criminal practise, and these were white. According to the physicians it is the patients themselves who induce abortion.

The country midwife labors under peculiar difficulties. She is not trained to recognize complications early and when emergencies arise it may take hours before a physician can arrive. One case of post partum hemorrhage was lost by a colored midwife who had been impressed by a doctor that under no circumstances must she introduce her hand or anything else into the birth canal. When the hemorrhage com-

menced she sent five miles to the nearest doctor who happened to be in attendance on a case three miles from home in a house where there was no telephone. That midwife is held in ill repute in the neighborhood because she refused to treat the complication herself. Those who assume any responsibility and are most officious—usually the white midwives—are the most popular. One of this type naïvely stated that she always removed the placenta manually, immediately after the birth of the child, because she thought it was so much better for the mother. She also repaired perineal tears.

The colored midwives are spoken of as "grannies." The plane on which they are held is shown by the fact that when they are too old for any other work they become midwives. For the most part the colored midwife attempts less than the white and her practise is, perhaps, more easily guided by the physician, whereas, the white midwife has much more initiative and is more likely to compete with the physician for obstetrical cases.

The white midwives who have the largest practises and receive the highest fees live in or near the towns.

The following are some of the practises of a few colored midwives:

1. *Treatment for hemorrhage.*—Ice held in the hand; licking alum; a hot potato held in the hand; equal parts of paregoric and laudanum by mouth while at the same time a piece of cloth is burned in the stove; packing the vagina with any kind of rags that are handy in case of post partum bleeding.

2. *Treatment for delayed placenta.*—Feathers burnt under the nose of the patient to make her sneeze; salt held in the hands to make them sweat while the patient blows into a bottle.

3. *The use of douches and ergot.*—In one neighborhood ante partum douches were routine. Post partum douches are quite commonly used when the placenta is not intact or when the lochia have an abnormal odor. The midwife carries from patient to patient her own douche tip, which she greases before using. Ergot is used by a few of the white midwives to increase labor pains.

4. *The kinds of pads used.*—Anything from greased rags to burlap is used by the very poor unless the midwife is in a position to furnish them with something different. On one occasion we visited a poor Lithuanian woman who had been delivered that morning in a room containing two dilapidated beds and a broken chair. The midwife whom we accompanied informed us that a woman washing at a tub whom we could see from the window, had been confined the day before in the other bed. Our midwife not only received nothing for these confinements but even supplied these poor women with clean pads.

In our interviews we marveled at the intelligence of several of these colored midwives who had their training on plantations before the war and who to most of our questions gave replies which would have been a credit to the present generation. They formed a pleasant contrast to the one who in response to our request to see her license amiably produced her marriage license. Notwithstanding their superstition and ignorance the colored midwives were on the whole a simple-minded, sympathetic lot ready to trudge miles over the sandy roads in the midsummer heat to earn their meager fees which in many cases they never received at all.

In conclusion we feel that in the southern rural districts there is a special problem to solve. Most of the physicians in the country agree that the midwife cannot be dispensed with. The distances are too great for the number of physicians practising there and yet the fees are too small to support a greater number of physicians. Since the midwife seems to be a necessary evil in these southern districts the problem resolves itself into one of education. Yet unless the training and equipment were provided gratis the average colored midwife could not avail herself of it. Having had it would she be willing to continue to receive so small and uncertain a remuneration? At the present time the local physician must be looked to not to solve the problem, but for the palliation of these lamentable conditions and to encourage him there is demanded a closer supervision of the midwifery conditions existing in his community.

NOTES ON NEW BOOKS.

The Care of the Skin and Hair. By WILLIAM ALLEN PUSEY, M. D. (*New York and London: D. Appleton & Co., 1912.*)

This is a small book which can both with safety and profit be put in the hands of the laity. It contains much good advice, which if followed will save the pocketbooks of many seeking relief at the hands of quacks and beauty restorers. Dr. Pusey has written a book which is simple and has an attractive style adapted to the needs of the average intelligent reader.

Text-Book for Nurses: Anatomy, Physiology, Surgery and Medicine. By E. W. HEY GROVES, M. S., F. R. C. S. and J. M. FORTESCUE-BRICKDALE, M. A., M. D. (*London: Henry Frowde and Hodder & Stoughton, 1912.*)

The teaching of nurses, like the teaching of other classes of students, is not as yet well fixed along different paths, some instructors being anxious to give these women much more instruction than others think suitable. Up to a certain point the more nurses get the better as it thus fits them to fill creditably the many new fields of work that are opening to them. But when it is to be decided just how much anatomy or physiology is to be taught them, much depends on the teacher and the number of hours that are to be given to the subject in the school curriculum. This new text book of about four hundred large pages comprises the instruction in four fundamental subjects; eighty devoted to anatomy; somewhat less to physiology; nearly one hundred and fifty to surgery and less than one hundred to medicine. To the reviewer these proportions seem incorrect, for he feels that nurses have a greater need of thorough training in physiology and medicine than in anatomy and surgery, but so far as what the authors have to say on these four subjects, they have written a useful book. The subjects are treated simply but in a comprehensive way so as to give a nurse a good grasp of the branch she is studying. As the preface states: "The chief aim . . . . of the present book is to enable the nurse to understand the principles

underlying the medical and surgical treatment which it is her duty to assist in carrying out," and the authors have reached their goal in a satisfactory manner. It is hardly to be expected that this English work will be a standard text-book in any one of the American schools of nursing, but it is one which should be in the library of all such schools for nurses to refer to and study, for it is reliable and well written.

Stomatology in General Practice. A Text-Book of Diseases of the Teeth and Mouth for Students and Practitioners. By H. P. PICKERILL, M. D., etc. (*London: Henry Frowde and Hodder & Stoughton, 1912.*)

In this work the author has bridged over a "somewhat ill-defined territory lying between medicine and dentistry, which to many practitioners is to a certain extent a *terra incognita*." There is no doubt that this territory exists, and its recognition has led of late to the establishment of dental clinics in a few hospitals, and it is to be hoped that the number of these clinics will be rapidly increased. But where no clinics exist this book will be most helpful to both students and practitioners, especially surgeons, for the author is not only a skilful operator in difficult cases dealing with the teeth and jaws, but he also has written the kind of text-book which is needed by the profession; in other words it is well balanced and the pure internist, as well as the general surgeon, will benefit by its perusal. Dr. Pickerill describes inflammatory diseases of the mouth, the manifestation of systemic diseases in the mouth, oral sepsis and its effects, the relationship of oral disease to various lesions of the nervous system, caries of the teeth and its prevention, the surgical treatment of dental disease, fractures, dislocations, and closure of the jaws and oral tumors. These chapter headings indicate the general scope of the work, which is not too large, or covers too much ground. "Stomatology in General Practice" may be cordially recommended to those eager to have a good understanding of the troubles described.

Electrical Injuries: Their Causation, Prevention and Treatment. Designed for the Use of Practical Electrical Men. By CHARLES A. LAUFFER, M. D. 50cts. (*New York: John Wiley & Sons, 1912.*)

This little first-aid volume may assist electricians who are liable to burns or shocks from highly charged electrical apparatus, and also physicians who have not had the opportunity to learn how to treat electrical accidents, but it is a trifling work and padded with matter which has but slight connection with the subject under discussion.

Manual of Surgery. By ALEXIS THOMSON, F. R. C. S. Ed. and ALEXANDER MILES, F. R. C. S. Ed. Vols. II and III. Regional and Operative Surgery. Fourth Edition. (*Edinburgh, Glasgow and London: Henry Frowde and Hodder & Stoughton, 1912.*)

As a manual for students this surgery will appeal to a large class. The many chapters are well proportioned, the directions for operations are clear, and the illustrations serviceable; the size of the volume is such as to make it easy to carry about with one and the type is pleasing. These are all qualities to hold the reader. As an example of what a manual should be, this one ranks high and the authors are to be congratulated on having prepared so excellent a volume.

International Clinics. Vol II. 22nd Series. $2. (*Philadelphia and London: J. B. Lippincott Company, 1912.*)

A Symposium on Anaesthesia is doubtless the chapter in this volume which will be most extensively read, but there are other interesting shorter papers by Jackson, one of the very few really skilful operators with the bronchoscope in America, on "Direct Methods of Examination of the Larynx, Trachea, etc," and one by Baruch, who is an authority on hydrotherapy, on "The Management of Sunstroke—A Lesson in Hydrotherapy." Flexner's "Lecture on the Present Status of Epidemic Poliomyelitis" is also one to appeal strongly to the general practitioner.

No. 50. Scientific Memoirs. By Officers of the Medical and Sanitary Departments of the Government of India. *Preliminary Report on an Investigation into the Etiology of Oriental Sore in Canbay.* By CAPT. W. S. PATTON, M. B. Price 6 annas. (*Calcutta: Superintendent Government Printing, India, 1912.*)

The author after a careful investigation of sixty cases believes the Oriental Sore to be transmitted by the *Cimex rotundatus*, which fact, if proven by further investigations, will add another disease to the growing list of infections due to the bite of various insects.

Primary Malignant Growths of the Lungs and Bronchi. A Pathological and Clinical Study. By I. ADLER, M. D. $4. (*New York: Longmans, Green & Co., 1912.*)

Dr. Adler, after a careful search through the literature for the accounts of these growths, has prepared an important contribution to their history, of service both to physicians and surgeons. Only a small part of the volume is devoted to the pathology and clinical symptoms of the tumors, the remaining two-thirds being taken up by an exhaustive analysis of all the cases so far reported. Of these by far the larger number are carcimomata which outnumber the sarcomata by more than 4 to 1. The author has tabulated 375 of the former and 90 of the latter. Besides these there are 100 which are of doubtful origin, and 18 classified as miscellaneous. As a collective report on these oftentimes obscure growths this volume will serve as a most useful guide. As a piece of book-making it is unfortunately not so praise-worthy—it is printed on too heavy paper, and might have been reduced in size so as not to be so expensive.

The Medical Diseases of Children. By REGINALD MILLER, M. D. (Lond.), etc. 12/6. (*Bristol: John Wright and Sons, Ltd., 1911.*)

It is a difficult undertaking to discuss with entire satisfaction the medical diseases of children in a volume of this size.

The author's concise style has, however, enabled him to produce a small book of real value. It is practical, well illustrated and generally in keeping with the accepted facts and theories of modern teaching.

A few rather positive statements are made which would seem open to argument, for instance, that curd indigestion offers the greatest stumbling-block to artificial feeding and that the use of citrate of soda is the most effectual method of controlling this. For many years the digestion of the fats of cows' milk has been considered quite as difficult and more recently the work of Finkelstein has forced upon us the important and at times disastrous effect of sugars. The experience in this country, at least in the use of citrate of soda, has been generally disappointing. The arrangement of the book is in some respects unique—especially with regard to infectious diseases. The author, as far as possible, has attempted a classification based on the broader conception of the infecting organism, including under tuberculous infection the various manifestations of this disease, under pneumococcal infection, pneumococcal pneumonia, pleurisy, empyema, pericarditis, endocarditis, meningitis, otitis, peritonitis, etc., under the rheumatic infection, acute rheumatic fever, chorea, etc.

While necessarily incomplete in our present knowledge of bacteriology, such a classification is of particular value in connection with children's diseases in emphasizing, as the author states, the tendency toward generalization by bacterial infections in children.

The work throughout has the stamp of one writing from a wide personal experience and can be freely recommended to students and practitioners.

R. A. U.

Oxford Medical Publications. Salvarsan in Syphilis and Allied Diseases. By J. E. R. McDONAGH, F. R. C. S. $3. (*London: Henry Frowde and Hodder & Stoughton, 1912.*)

As a supplement to the System of Syphilis, in five volumes, under the editorship of Power and Murphy, published a short time since by the Oxford Press, the present volume has been prepared, and makes a fitting ending to the exhaustive and excellent system. McDonagh has had a large experience with the use of salvarsan and his advice is sound, though we cannot agree with him in thinking that primary chancres should be excised when possible. This treatise presents clearly but briefly the general principles underlying the administration, use, and results of salvarsan, and the general practitioner will find it a helpful guide.

Psychotherapy. By JAMES J. WALSH, M. D., etc. $6. (*New York and London: D. Appleton & Co., 1912.*)

There is much in this large volume to help the general practitioner and much that would help patients if presented under slightly different form. The book is a treatise on mind-cure, as exercised by the patient on himself, under the influence or suggestion of his physician. This is a form of cure to which, unfortunately for the patient, few physicians give the necessary time and, therefore, many a patient falls into the hands of quacks, or becomes a confirmed neurasthenic or worse, a burden to himself and his friends and the world about him. Dr. Walsh, after an introduction on psychotherapy in the history of medicine, discusses general psychotherapeutics in four chapters under general considerations, the individual patient, general principles, adjuncts and disturbing factors. He then takes up special psychotherapy as applied to diseases of the digestive tract, heart, lungs, gynecology, skin diseases, etc., and after dealing with the bodily functions, discusses disorders of the psyche under psychoneuroses, disorders of mind and will, and concludes his work of nearly eight hundred closely printed pages with a chapter on psychotherapy in surgery. As can be seen from this incomplete outline the author has attempted to cover nearly all medicine, and while he has written a work of real value from many points of view, with his usual skill and attractive style, yet the work is longer than it need be. There is much repetition as is inevitable in composing such a volume, for suggestions that will help a patient in one disease are in most instances the same as will help him in another disorder, so that it seems hardly worth while to divide psychotherapy into so many sections as the author has done. There are many points to which exception might be taken, but as they do not really affect the value of the work, they may as well be left unnoted, except to indicate that the work is written by an excellent general practitioner who draws more from his own experience than from the more exact conclusions that are being arrived at by the best students of psychology and psychiatry. "Psychotherapy" is a work which fills excellently a hole that has remained empty up to now on the doctor's bookshelves and should be found in every practitioner's library if only to call his attention constantly to this form of therapeutics, which is the best of all in many cases.

Progressive Medicine. Edited by HOBART AMORY HARE, M. D., assisted by LEIGHTON F. APPLEMAN, M. D. Vol II. (*Philadelphia and New York: Lea & Febiger, June, 1912.*)

This volume deals with hernia, the surgery of the abdomen exclusive of hernia, gynecology, diseases of the blood, spleen, thyroid gland, nutrition, lymphatic system, and diathetic and metabolic diseases and ophthalmology. It is always interesting to note the amount of literature on hernia, such an ancient topic, and one which would appear as fairly well settled, and yet which so constantly demands fresh consideration. Very naturally cancer of the uterus takes up more space in this volume than any other topic, since there are so many questions in regard to it that remain to be solved. The various chapters are carefully prepared and the few illustrations well chosen.

At the request of Messrs. John Wright & Sons, Ltd. (Bristol, England), we desire to state that they have disposed of the American Market for Dr. Herbert French's Index of Diagnosis to Messrs. William Wood & Co., of New York. We regret that the American publishers did not receive credit for this in our notice of the work in the May issue of the BULLETIN.

Die experimentelle Bakteriologie und die Infektionskrankheiten mit besonderer Berücksichtigung der Immunitätslehre. Von DR. W. KOLLE und DR. H. HETSCH. Dritte, erweiterte Auflage. $8.50. (*Berlin and Wien: Urban & Schwarzenberg; New York: Rebman Company, 1911.*)

The third edition of this text-book of Kolle and Hetsch deserves more than a passing notice for a number of reasons. It is in many ways the most comprehensive of the German text-books in Bacteriology and the 1911 edition has been brought thoroughly up to date, including possibly the most of the important advances in the knowledge of this subject which have been made since the appearance of the earlier edition. Its two volumes, comprising together nearly a thousand pages, make it too voluminous and detailed for any but advanced students in bacteriology, and the book, therefore, must be regarded as peculiarly fitted for special workers in this field. The form or arrangement of the material presented is unique. Each special topic is considered in a lecture (*Vorlesung*), there being altogether fifty-nine of such lectures. These vary in length from five to twenty-five pages depending upon the nature of the subject, special lectures being devoted, for instance, to the antitoxins, to the cytotoxins, to methods of serum-diagnosis, and to the principal infectious diseases—anthrax, cholera, typhoid fever, dysentery, malta fever, meningitis, etc. The book is not merely bacteriological in scope, however, since the second volume takes up such diseases as diphtheria, tuberculosis and the protozoan infections, including amoebic dysentery, trypanasomiasis, malaria, and Texas fever. In addition a number of diseases of unknown etiology, such as rabies and small-pox, are considered in detail with an accurate discussion of the several theories which have been advanced to explain their etiology.

Despite the excellent arrangement of the material presented and the careful discrimination which the authors have employed in the selection of the subject matter, in certain particulars the book deserves severe criticism. Throughout both volumes there is an almost absolute disregard of the work of American investigators. In consequence some of the most notable advances in bacteriology and epidemiology of the past few years have not been mentioned. Thus in the chapter on leprosy nothing is said as to the cultivation of the leprosy bacillus by Musgrave and Clegg and by Duval, and in the bibliography attached to this chapter the names of these investigators do not appear. On page 468 of Volume I the definite statement is made that "the cultivation of the leprosy bacillus has not yet been accomplished," and yet the authors have had at least two years to find out about this most important work. Again, slightly less than a page is devoted to typhus fever and no reference is made to the wonderful achievements of Ricketts, Anderson, and Goldberger in Mexico and of Nicolle in Tunis upon the production of this disease in apes and upon the rôle of the body louse in the transmission of the infection from person to person. If the short period of time which has elapsed since the publication of this work and the ap-

pearance of the third edition of Kolle and Hetsch may be put forward as an excuse for the failure of the authors to take account of the recent discoveries on leprosy and typhus fever, the same excuse cannot be used in regard to the failure to mention MacCallum and Opie in the chapter on malaria and Councilman in the chapter on small-pox. While such errors can be regarded as errors of omission, no justification, whatever, can be proposed for the adoption of Fraenkel's name, *bacillus phlegmones emphysematosæ*, for the *bacillus aerogenes capsulatus* of Welch and Nuttall and the statement that this organism was more accurately described by Fraenkel than by the American bacteriologists.

These are but a few examples of the many failures in Kolle and Hetsch's text-book to recognize work done on this side of the Atlantic Ocean, but they serve to indicate how the neglect to carefully review American literature has permitted the introduction of serious errors in the subject matter of which the two volumes are composed. One wonders, indeed, whether the authors are not actuated by the desire to Germanize the entire science of bacteriology, since one reads with surprise on page 852, Volume 2, of the work of "Brinckeshoff and Tyzzu" in Manila only to realize that these names refer to two well-known members of the staff of Harvard University.

Despite these mistakes in this publication, which we feel compelled to mention out of loyalty to American science, the work is thorough, comprehensive and well arranged, the subject matter is carefully chosen, and the two volumes will appeal deeply to all thoughtful students of bacteriology and protozoölogy.

A Manual of Materia Medica for Medical Students. By E. Quinn Thornton, M. D. $3.50. (*Philadelphia and New York: Lea and Febiger, 1911.*)

This is an excellent work which takes up what is usually regarded as rather a dry subject in a clear way. Particularly valuable are the sections on the methods of administration of drugs. The work deals only with the preparations which are in the United States Pharmacopeia and it is a question whether some additions would not add to the value of the book. For example, under digitalis it would be an advantage to find some reference, which need not be extensive, to preparations other than those in the pharmacopeia. It is not always easy for the student to know where to search for information regarding digipuratum, for example. Some of the preparations of arsenic might be cited as another example of this. Doubtless the author considered this and had good reasons for his decision. Perhaps it might be difficult to know where to draw the line and decide what was worthy of mention. One point caught the reviewer's attention, namely, the description of the composition of Blaud's pills. This is given as consisting of carbonate of iron and excipients only. This mistake occurs in several American text-books. The special value of Blaud's mass is that it is a combination of potassium and iron which seems to be more efficient than the iron alone. This is a small matter but the mistake is so common that it is worth drawing attention to it. We can heartily recommend this work as an excellent text-book on materia medica.

Immunity. Methods of Diagnosis and Therapy and their Practical Application. By Dr. Julius Citron. Translated and edited by A. L. Garbat. Illustrated. $3. (*Philadelphia: P. Blakiston's Son & Co., 1912.*)

This work is intended "to serve a purely practical purpose"; to review briefly "in a purely critical form the various methods of immunity diagnosis, especially those relating to tuberculosis and syphilis." This aim it very well fulfils. The extensive experience of the author both in the laboratory and in the clinic enables him to sift out the essential facts, and to indicate their significance and relative importance. The various laboratory methods of serum diagnosis are simply and briefly explained, in all their essential details. Especially commendable is the emphasis laid on the necessary control experiments. In addition the theories forming the basis of the various tests are critically discussed, but perhaps too briefly.

While intended primarily for the laboratory worker the book should also be helpful to the practising physician in explaining the significance of the reactions and in pointing out just what conclusions may be drawn from positive and negative reactions. The chapters on tuberculin are of special interest. Consideration is given both to its therapeutic and diagnostic use, and the contraindications are carefully outlined. The therapeutic use of sera and vaccines is also briefly considered.

The chief criticisms to be offered are that in places the text is too brief for clearness; that the English at times is a little involved, and that too much of the German idiom has been retained in the translation.

The work is an excellent one and should prove to be of great practical value.

P. W. C.

Parasitic Amœbæ of Man. By Charles F. Craig, M. D., Captain Medical Corps, United States Army. From the Bacteriological Laboratory of the Army Medical School, Washington, D. C., and the Rockefeller Institute for Medical Research, New York City. $2.50. (*Philadelphia: J. B. Lippincott Company, 1911.*)

This volume is a splendid addition to our medical literature and is probably the best treatise in English on a much neglected, but equally important, subject. A brief historical resumé shows how recent is our knowledge of amœbiasis; one notes that Osler is mentioned as the first clinician in America to observe amœbæ in a case of dysentery, in 1890; while to the monograph of Councilman and Lafleur is ascribed much of the stimulus for work on the subject subsequent to the year 1891. Three chapters cover well the biology, nomenclature, classification, and methods for the indentification of amœbæ in general; adequate space is given over to the details of fixation and staining, though for the routine purpose of diagnosis, the value of the examination of fresh specimens, supplemented by intravitam staining with neutral red is well emphasized. The following chapter goes to uphold the author's view "that the parasitic amœbæ of man have not been cultivated."

About 130 pages are then rightly devoted to a minute description of those amœbæ suspected or convicted of causing dysentery in man; namely, the entamœba coli, histolytica and tetragena, and an excellent summary gives in tabulated form those diagnostic points which should enable any careful observer to differentiate the three forms. This is an extremely important thing, not least of all from the stand-point of therapy, when we realize that "if the entamœba coli were the cause of a form of dysentery, practically 50 per cent of all individuals in nearly every locality would suffer from this disease." That the entamœba histolytica *is* the cause of true amœbic dysentery is well emphasized in the section describing the pathology of the disease. Further evidence is advanced to show that the less well known entamœba tetragena and the more recently described paramœba hominis may be blamed for some true cases of dysentery. Several other forms of intestinal amœbæ are briefly mentioned, but the validity of their rights to be classed as distinct pathogenic forms is, in all instances as yet, doubtful. Amœbæ of the mouth, genitourinary tract, exudations, abscesses, and of the lungs, are concisely dealt with. A list of 122 references completes the work, which is excellent as regards printing, illustrations, and a singular absence of typographical errors.

The book will undoubtedly prove of immense value to biologists, workers in clinical laboratories, and to all students in the field of internal medicine.

The Growth of Bone: Observations on Osteogenesis. An Experimental Inquiry into the Development and Reproduction of Diaphyseal Bone. By WILLIAM MACEWEN, F. R. S. Glasgow. $2.25. (*James Maclehose and Sons, 1912.*)

This book in an extremely interesting attack on one of the generally accepted tenets of surgery, the belief that periosteum is the essential factor in the reproduction of adult bone, and that diaphyseal bone denuded of its periosteum will die. In the preface, the author states his purpose to show this belief to be fallacious, and the whole volume is a narrative of many clinical cases of great interest, supported by a large number of experiments, all bearing more or less closely on the point at issue.

Macewen holds that bone formation is the result of the life process of the osteoblast, that the adult osteoblast may, under stimulating circumstances, such as fracture or inflammation, regain its embryonic activity, and that when it does so, it possesses at least as great vegetative powers as the epithelial cell. Hence any fragment of bone containing living osteoblasts may become a center of new bone growth, and bone is, therefore, an easily transplantable or graftable tissue. But the writer holds that normal periosteum contains no osteoblasts, and hence has no power or influence whatever in the regeneration of bone. He grants that when osteomyelitis occurs, the periosteum displays bone-forming ability, but explains it thus: The inflammatory process causes a proliferative reaction on the part of the osteoblasts, which are crowded outward into the periosteum. Were the periosteum not present they would invade the surrounding soft parts and cause an osseous infiltration of muscles, etc. Hence periosteum, instead of being a bone-forming structure, is really a limiting membrane, which checks bone over-growth. When it has become itself infiltrated with osteoblasts as a result of pathological processes, and is then stripped up or transplanted, it displays the power of regenerating bone, but such a power is absent in the case of normal periosteum. Numerous experiments and clinical citations make one feel that the author is well sustained in his contention.

On critical reflection one is led to feel that Macewen's point of view is, perhaps, not so revolutionary as it appears at first sight. His consideration of the whole subject is based on the definition of periosteum as the outer layer of fibrous tissue, connected with the bone proper by loose areolar tissue and free from osteoblasts normally in adult life. While such a definition may be histologically correct, there is no doubt that the surgeon in dealing with what he considers periosteum, and using considerable force to detach it with a semi-sharp instrument, must remove more than Macewen's layer. In fact, in certain of Macewen's experiments where transplanted periosteum developed nodules of bone, he explained that occurrence by the fact that probably a minute flake of bony tissue had been removed with the periosteum. There can be no doubt that periosteum, as removed clinically, frequently contains such particles of bone. Hence one can hardly attach to the conclusions of Macewen the extensive clinical weight they might otherwise deserve.

The book is illustrated profusely with excellent plates, and is well indexed. The style of the writer, as is usual with British authors, is faultless. The book is full of stimulus and suggestion, and represents many years of careful observation and hard work.

H. B. S.

The Stomach, Intestines and Pancreas. By W. C. BOSANQUET, M. D., and H. S. CLOGG, M. S. Edited by JAMES CANTLIE, M. B. (*New York: William Wood & Co., 1912.*)

In this work we have an attempt to discuss the diseases concerned from both the medical and surgical aspects. Such an effort in the scope of a small volume can only hope to be successful in so far as is permitted by the limitations of space. The authors on the whole have succeeded in giving a clear summary of the subject. There are two questions connected with disease of the intestinal tract on which opinion is as widely different on the two sides of the Atlantic as they are apart geographically. These are mucous colitis and appendicitis. The essential point in the etiology of mucous colitis which is most important for proper treatment is the recognition of the fact that it is nearly always secondary to a general nervous disturbance. Unless this can be remedied the local condition is not permanently benefited. Yet in the discussion of treatment in this work no reference is made to this fact and it is small wonder that the authors speak of treatment as being unsatisfactory. Of course it is if the cause is not recognized and remedied. The treatment of appendicitis as given here is most unsatisfactory. To give as the indication for operation in ordinary acute appendicitis the recognition of a spreading peritonitis deserves strong condemnation. It would be interesting to ask the authors how often they have regretted operating too early and how often too late in an acute case. It is quite correct as they say that "the majority of cases of appendicitis will subside," but what about the minority which will not subside and in which delay often means death? In most diseases the *majority* recover; our fight is to save some of the minority.

Despite these points which deserve criticism, there is much in the work to be commended, its limitations always being recognized.

Augustus Charles Bernays. A Memoir. By THEKLA BERNAYS. $2. (*St. Louis: C. V. Mosby Company, 1912.*)

Those who only knew Bernays as a brilliant surgeon will be glad to read this account of him by his sister and learn the kind of man he was. The memoir is frank and does not conceal the man's failings—this is as Bernays would have had it, for he was fearless, frank, and indifferent to the common judgment of men. He was never married and for many years lived and traveled much with his sister. Born of German parents he had all the characteristic German family feeling and was devoted to her, who, equally devoted to him, has written a brief story of his life. Allowing for the natural overflow of a sister's feelings for her brother, who was so fine a surgeon, and had so much kindliness of heart, this memoir portrays him vividly, and the reader is left with an empression of a man big in many ways.

Methods of Organic Analysis. By HENRY C. SHERMAN, Ph. D. Second edition, rewritten and enlarged. $2.40. (*New York: The Macmillan Company, 1912.*)

The first edition of this work was favorably commented upon in our columns (May, 1906), and the new edition demands also a word of praise. The author in enlarging his original work has done so with skill, so that its use as a text-book is unimpaired in this respect, and the new chapters add important material for students, to whom the work can be warmly commended.

Clinical Disorders of the Heart Beat. A Handbook for Practitioners and Students. By THOMAS LEWIS, M. D. $2. (*London: Shaw and Sons; New York: Paul B. Hoeber, 1912.*)

The purpose of this little book is to acquaint the general practitioner with the essential facts which researches by means of graphic methods in the study of the heart-beat have contributed to the practice of medicine and to enable him to make practical use of these data without having to resort to the more elaborate methods of diagnosis.

The book opens with an introductory chapter upon the general characteristics of the principal types of cardiac disorder encountered clinically: Sinus arrhythmia, heart-block, premature contractions, paroxysmal tachycardia, auricular fibrillation, alternation of the pulse. The subsequent chapters are devoted to a concise discussion of the main clinical characteristics, diagnosis, prognosis and treatment of each of these forms. No attempt is

made to give references or the names of investigators in the subject. Etiological factors encountered by the author in a large series of his own cases are given in tabular form, and the course of the abnormal impulses within the heart is indicated by very simple diagrams.

In the clinical diagnosis of arrhythmias, the author calls attention to the characteristics of the heart sounds and radial pulse, by which fairly accurate functional diagnoses may be made in a considerable number of cases. Inspection of the pulsation over the jugular veins, however, does not receive adequate attention, although by this simple method, in the reviewer's experience, the practitioner's accuracy and refinement of diagnosis may be greatly increased.

The discussion of heart-block is in the main excellent. One statement of the author is worthy of comment. He writes that the milder forms of heart-block "often require digitalis medication, and this will frequently increase the grade of block. But the increase of block should not deter digitalis administration for the relief of dilatation, dropsy or other symptoms, nor is it in itself detrimental, the drug or its allies may be given without restraint and often beneficially." This is in direct contrast to the almost universal clinical experience and the experiments of v. Tabora which indicate administration of digitalis in cases of *partial* heart-block often suddenly cuts off all conduction and precipitates attacks of syncope before the cumulative action of the drug can affect the ventricular muscle sufficiently to increase its automaticity. The experience of most observers is that the use of digitalis is almost always contraindicated in partial block and indicated after complete block has once become established. As might be expected from the experimental work of the writer, the subject of auricular fibrillation is particularly well discussed in all its phases.

The style of the book is clear, direct and fluent, and the book may be commended to the general practitioner who desires a small monograph upon this phase of the subject.

A. D. HIRSCHFELDER.

The Theory of Schizophrenic Negativism. By PROFESSOR E. BLEULER. Translated by WILIAM A. WHITE, M. D. 60 cts. (*New York: The Journal of Nervous and Mental Disease Publishing Company, 1912.*)

Dr. White, the Superintendent of the Government Hospital for the Insane, Washington, D. C., who has himself contributed two noteworthy monographs to this series published by The Journal of Nervous and Mental Disease, again puts the profession under obligation to him by this skilful translation of Dr. Bleuler's brief paper. Psychiatrists who do not read German fluently will be especially grateful for the publication of this important article to which we are glad to call attention.

BOOKS RECEIVED.

The International Medical Annual. A Year Book of Treatment and Practitioner's Index. Thirtieth Year, 1912. 8vo. 654 pages. E. B. Treat & Company, New York.

Report to the London School of Tropical Medicine on Investigations on Dysentery in Fiji During the Year 1910. By P. H. Bahr, M. A., M. B., B. C., D. T. M. & H., Cantab., M. R. C. S., Eng., L. R. C. P. (Lond.). Together with an Account of the Occurrence and Spread of Dysentery in the Pacific in Former Years by B. Glanvill Corney, I. S. O., M. R. C. S. With coloured and monochrome plates and many charts. 1912. 4to. 77 pages. Witherby & Co., London.

Compendium of Diseases of the Skin. Based on an Analysis of of Thirty Thousand Consecutive Cases with a Therapeutic Formulary. By L. Duncan Bulkley, A. M., M. D. Fifth revised edition of the Manual of Diseases of the Skin. 1912. 8vo. 286 pages. Paul B. Hoeber, New York.

New and Nonofficial Remedies, 1912. Containing Descriptions of the Articles Which Have Been Accepted by the Council on Pharmacy and Chemistry of the American Medical Association Prior to Jan. 1, 1912. 12mo. 298 pages. American Medical Association, Chicago.

A Manual of Clinical Chemistry, Microscopy, and Bacteriology. By Dr. M. Klopstock and Dr. A. Kowarsky. Only authorized translation from the last German edition, thoroughly revised and enlarged. Illustrated with forty-three textual figures and sixteen colored plates. [1912.] 12 mo. 371 pages. Rebman Company, New York.

The Technique and Results of Radium-Therapy in Malignant Disease. By M. Dominici, M. D. and A. A. Warden, M. D. Reprinted from "The British Medical Journal" of August 27, 1910, with additional Plates and more recent Notes, March, 1912. 8o. 1912. 29 pages. J. & A. Churchill, London.

Diseases of the Eye. By J. Herbert Parsons, D. Sc., M. B., B. S., F. R. C. S. Second edition. 1912. 8vo. 684 pages. P. Blakiston's Son & Co., Philadelphia.

Duodenal Ulcer. By B. G. A. Moynihan, M. S. (Lond.), F. R. C. S. Second edition, enlarged. Illustrated. 1912. 8vo. 486 pages. W. B. Saunders Company, Philadelphia and London.

Post-Mortems and Morbid Anatomy. By Theodore Shennan, M. D., F. R. C. S. Edin. 1912. 8vo. 496 pages. Constable and Company, Limited, London.

Tumors of the Jaws. By Charles Locke Scudder, M. D. With 353 illustrations, 6 in colors. 1912. 8vo. 391 pages. W. B. Saunders Company, Philadelphia and London.

Pellagra. An American Problem. By George M. Niles, M. D. Illustrated. 1912. 8vo. 253 pages. W. B. Saunders Company, Philadelphia and London.

Modern Methods in Nursing. By Georgiana J. Sanders. With 228 illustrations. 1912. 12 mo. 881 pages. W. B. Saunders Company, Philadelphia and London.

The British Guiana Medical Annual for 1910. Edited by K. S. Wise, M. B., B. S., B. Sc. (Lond. Univ.), D. P. H., M. R. C. S. (Eng.), L. R. C. P. (Lond.). 1912. 8vo. XCVI+126 pages. "The Argosy" Company, Limited, Demerara.

Studies from the Rockefeller Institute for Medical Research. Reprints. Volume XIV. 1912. 8vo. The Rockefeller Institute for Medical Research, New York.

University of Pennsylvania. Sixth Annual Report of the Henry Phipps Institute. For the Study, Treatment and Prevention of Tuberculosis. February 1, 1908 to February 1, 1910. 4to. 1912. 137 pages. Henry Phipps Institute, Philadelphia.

Augustus Charles Bernays. A Memoir. By Thekla Bernays. 1912. 12mo. 309 pages. C. V. Mosby Company, St. Louis.

Psychotherapy. Including the History of the Use of Mental Influence, Directly and Indirectly, in Healing and the Principles for the Application of Energies Derived from the Mind to the Treatment of Disease. By James J. Walsh, M. D., Ph. D. 1912. 8vo. 806 pages. D. Appleton and Company, New York and London.

Scientific Memoirs. New Series No. 48 By Officers of the Medical and Sanitary Departments of the Government of India. *Investigations into the Jail Dietaries of the United Provinces.* By Major D. McCay, M. B., M. R. C. P., I. M. S. 1912. 4to. 200 pages.

No. 49. Epidemic Dropsy in Calcutta. Being the Final Report of an Enquiry Carried out by Major E. D. W. Greig, M. D., D. Sc., I. M. S. 1912. 4to. 79 pages. Superintendent Government Printing, Calcutta, India.

No. 50. Preliminary Report on an Investigation into the Etiology of Oriental Sore in Cambay. By Captain W. S. Patton, M. B., I. M. S. 1912. 4to. 41 pages. Superintendent Government Printing, Calcutta, India.

Primary Malignant Growths of the Lungs and Bronchi. A Pathological and Clinical Study. By I. Adler, A. M., M. D. 1912. 8vo. 325 pages. Longmans, Green and Co., New York, London, Bombay, and Calcutta.

Association Tests. Being a Part of the Report of the Committee of the American Psychological Association on the Standardizing of Procedure in Experimental Tests. By R. S. Woodworth and Frederic Lyman Wells. The Psychological Monographs. Edited by James Rowland Angell, Howard C. Warren, John B. Watson and Arthur H. Pierce. Vol. XIII. No. 5. December, 1911. 8vo. 85 pages. Psychological Review Company, Princeton, N. J., Baltimore, Md., and Lancaster, Pa.

Public Health, Chemistry and Bacteriology. A Handbook for D. P. H. Students. By David McKail, M. D. (Glasg.), D. P. H. (Camb.), F. R. F. P. S. G. 1912. 12°. 409 pages. John Wright & Sons Ltd., Bristol; Simpkin, Marshall, Hamilton, Kent & Co. Ltd., London.

Sprue: Its Diagnosis and Treatment. By Charles Begg, M. B., C. M. Edin. Illustrated. 1912. 8vo. 124 pages. John Wright & Sons, Ltd., Bristol; Simpkin, Marshall, Hamilton, Kent & Co. Ltd., London.

The Healthy Baby. The Care and Feeding of Infants in Sickness and in Health. By Roger H. Dennett, M. D. 1912. 12mo. 235 pages. The Macmillan Company, New York.

Biennial Report of the Louisiana State Board of Health. To the General Assembly of the State of Louisiana, 1910-1911. 8vo. 261 pages. New Orleans.

Bulletin of Iowa Institutions. (Under the Board of Control). Published Quarterly. Volume XIII. 1911. 8vo. 308 pages. Des Moines, Iowa.

Progressive Medicine. A Quarterly Digest of Advances, Discoveries and Improvements in the Medical and Surgical Sciences. Edited by Hobart Amory Hare, M. D., assisted by Leighton F. Appleman, M. D. Volume II. June, 1912. 8vo. 391 pages. Lea & Febiger, Philadelphia and New York.

Transactions of the New York Obstetrical Society. Volume for 1909-1911. Reprinted from the American Journal of Obstetrics. [1912.] 8vo. 488 pages. William Wood & Company, New York.

A System of Treatment. By Many Writers. Edited by Arthur Latham, M. A., M. D., Oxon.; F. R. C. P. Lond.; and T. Crisp English, M. B., B. S. Lond.; F. R. C. S. Eng. Volumes I and II. General Medicine and Surgery. Volume III. Special Subjects. Volume IV. Obstetrics and Gynæcology. 1912. 8vo. The Macmillan Company, New York.

Commonwealth of Pennsylvania. The Fourth Annual Report of the Commissioner of Health. Parts I and II. 1909. 8vo. 1619 pages. 1911. Harrisburg.

Quain's Elements of Anatomy. Eleventh edition. Editors: Edward Albert Schäfer, LL. D., Sc. D., M. D., F. R. S., Johnson Symington, M. D., F. R. S., Thomas Hastie Bryce, M. A., M. D. In Four Volumes. Vol. II. Part I. Microscopic Anatomy. By E. A. Schäfer. With 1001 engravings, and 21 coloured plates. 1912. 8vo. 739 pages. Longmans, Green, and Co., London, New York, Bombay, and Calcutta.

Medical Education in Europe. A Report to the Carnegie Foundation for the Advancement of Teaching. By Abraham Flexner. With an Introduction by Henry S. Pritchett. Bulletin Number Six. 1912. 4to. 357 pages. New York City.

Transactions of the American Pediatric Society. Twenty-third Session held at Lake Mohonk, N. Y. May 31 to June 2, 1911. Edited by Linnaeus Edford La Fétra, M. D. Volume XXIII, 1911. 8vo. 388 pages. American Medical Association Press, Chicago.

La Tuberculose Inflammatoire. Par A. Poncet et R. Leriche. Avec 55 figures dans le texte. 1912. 16°. 604 pages. Octave Doin et Fils, Paris.

A Clinical Study of Acute Poliomyelitis. By Francis W. Peabody, M. D., George Draper, M. D., and A. R. Dochez, M. D. Monograph of the Rockefeller Institute for Medical Research. Number 4, June 1, 1912. 4°. 187 pages. The Rockefeller Institute for Medical Research, New York.

Methods of Organic Analysis. By Henry C. Sherman, Ph. D. Second edition, re-written and enlarged. 1912. 8vo. 407 pages. The Macmillan Company, New York.

Oxford Medical Publications. Henry Frowde, London; Hodder & Stoughton, London.

1. *Manual of Surgery.* By Alexis Thomson, F. R. C. S. Ed. and Alexander Miles, F. R. C. S. Ed. Volume third, Operative Surgery. With 220 illustrations. 1912. 12°. 565 pages.

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Transactions of the American Urological Association. Tenth Annual Meeting at Chicago, Illinois, September 26 and 27, 1911. Edited by Charles Greene Cumston, M. D. 1912. 8vo. 384 pages. Riverdale Press, Brookline, Mass.

Die physikalische Therapie der Gelenkkrankheiten. Von Dr. Eduard Weisz. Mit 83 Textabbildungen. 1912. 12°. 265 pages. Urban & Schwarzenberg, Berlin & Wien.

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The Theory of Schizophrenic Negativism. By Professor Dr. E. Bleuler. Translated by William A. White, M. D. Nervous and Mental Disease Monograph Series No. XI. 1912. 8vo. 36 pages. The Journal of Nervous and Mental Disease Publishing Company, New York.

Franklin's Contribution to Medicine. Being a Collection of Letters Written by Benjamin Franklin Bearing on the Science and Art of Medicine and Exhibiting His Social and Professional Intercourse with Various Physicians of Europe and America. By Theodore Diller. 1912. 8vo. 89 pages. Albert T. Huntington, Brooklyn, New York.

Electrical Injuries: Their Causation, Prevention and Treatment. By Charles A. Lauffer, A. M., M. D. First edition. First thousand. 1912. 16°. 77 pages. John Wiley & Sons, New York: Chapman & Hall, Limited, London.

International Clinics. A Quarterly of Illustrated Clinical Lectures and Especially Prepared Original Articles. Edited by Henry W. Cattell, A. M., M. D. Twenty-second Series. Volume II. 1912. 8vo. 316 pages. J. B. Lippincott Company, Philadelphia and London.

Public Health Reports. Issued in Weekly Numbers by the Surgeon General of the Public Health and Marine-Hospital Service of the United States. Volume XXVI. Part 1. January-June, 1911. 8vo. 1055 pages. Government Printing Office, Washington.

Studies in Cancer and Allied Subjects. Pathology. Conducted under the George Crocker Special Research Fund at Columbia University. Volume II. 1912. Fol. vi + 267 pages. The Columbia University Press, New York.

The Sexual Life of the Child. By Dr. Albert Moll. Translated from the German by Dr. Eden Paul. With an Introduction by Edward L. Thorndike. 1912. 8vo. 339 pages. The Macmillan Company, New York.

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The Surgical Clinics of John B. Murphy, M. D., at Mercy Hospital, Chicago. Volume I. Number 3. June, 1912. 8vo. 293-466 pages. W. B. Saunders Company, Philadelphia and London.

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